(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
2 March 2006 (02.03.2006)

PCT

(10) International Publication Number
WO 2006/021418 A1

(51) International Patent Classification:
A61K 31/4184 (2006.01) *A61P 9/00* (2006.01)
A61K 31/425 (2006.01) *A61P 9/10* (2006.01)
A61K 31/4439 (2006.01) *A61P 11/00* (2006.01)
A61K 31/445 (2006.01) *A61P 11/06* (2006.01)
A61K 31/4709 (2006.01) *A61P 17/00* (2006.01)
A61P 1/00 (2006.01) *A61P 19/02* (2006.01)
A61P 1/04 (2006.01) *A61P 27/02* (2006.01)
A61P 5/00 (2006.01)

(21) International Application Number:
PCT/EP2005/009083

(22) International Filing Date: 23 August 2005 (23.08.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
PCT/EP2004/009521
26 August 2004 (26.08.2004) EP

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: 2-SULFANYL-BENZOIMIDAZOL-1-YL-ACETIC ACID DERIVATIVES AS CRTH2 ANTAGONISTS

(57) Abstract: The invention relates to 2-sulfanyl-benzoimidazol-1-yl-acetic acid derivatives and their use as potent "chemoattractant receptor-homologous molecule expressed on Th2 cells" antagonists in the treatment of prostaglandin mediated diseases, to pharmaceutical compositions containing these derivatives and to processes for their preparation.

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2-SULFANYL-BENZIMIDAZOL-1-YL-ACETIC ACID DERIVATIVES AS CRTH2 ANTAGONISTS

The present invention relates to 2-sulfanyl-benzoimidazol-1-yl-acetic acid derivatives and their use as potent "chemoattractant receptor-homologous molecule expressed on Th2 cells" (hereinafter called CRTH2) antagonists in the treatment of prostaglandin mediated diseases, to pharmaceutical compositions containing these derivatives and to processes for their preparation. In particular, such derivatives may be used in pharmaceutical compositions for the treatment of both chronic and acute allergic/immune disorders comprising allergic asthma, rhinitis, chronic obstructive pulmonary disease (COPD), dermatitis, inflammatory bowel disease, rheumatoid arthritis, allergic nephritis, conjunctivitis, atopic dermatitis, bronchial asthma, food allergy, systemic mast cell disorders, anaphylactic shock, urticaria, eczema, itching, inflammation, ischemia-reperfusion injury, cerebrovascular disorders, pleuritis, ulcerative colitis, eosinophil-related diseases, such as Churg-Strauss syndrome and sinusitis, basophil-related diseases, such as basophilic leukemia and basophilic leukocytosis in humans and other mammals.

Prostaglandin D2 is a known agonist of the thromboxane A2 (TxA2) receptor, the PGD2 (DP) receptor and the recently identified G-protein-coupled "chemoattractant receptor-homologous molecule expressed on Th2 cells" (CRTH2).

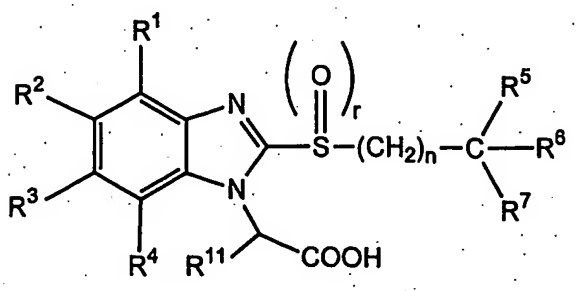
The response to allergen exposure in a previously sensitized host results in a cascade effect involving numerous cell types and release of a number of cytokines, chemokines, and multiple mediators. Among these critical initiators are the cytokines interleukin (IL)-4, IL-13, and IL-5, which play critical roles in Th2 cell differentiation, immunoglobulin (Ig)E synthesis, mast cell growth and differentiation, upregulation of CD23 expression, and the differentiation, recruitment, and activation of eosinophils. The stimulated release of the array of mediators, causes end-organ damage, including constriction and hyperresponsiveness, vascular permeability, edema, mucous secretion, and further inflammation.

Because of the number of responses targeted, corticosteroids have proven to be the most effective therapy. Rather than antagonizing these specific responses in a directed way, another approach is to alter the immune response, that is, to change the nature of the immunological response to allergen. CRTH2 is preferentially expressed on Th2 cells and is a chemoattractant receptor for PGD2 that mediates PGD2-dependent migration of blood Th2 cells. Chemoattractants are responsible for the recruitment of both Th2 cells and other effector cells of allergic inflammation and may provide the conceptual basis for the development of new therapeutic strategies, especially in allergic conditions.

So far, few compounds having CRTH2 antagonistic activity have been reported in the patent literature. In GB Patent Specification No. 2388540 Bayer AG claims the use of Ramatroban ((3R)-3-(4-fluorobenzene-sulfonamido)-1,2,3,4-tetrahydrocarbazole-9-propionic acid) for the prophylaxis and treatment of allergic diseases, such as asthma, allergic rhinitis or allergic conjuvatitis. Further, (2-*tert.*-butoxycarbonyl-1, 2, 3, 4-tetrahydro-pyrido[4,3-b]indol-5-yl)-acetic acid and (2-ethoxycarbonyl-1, 2, 3, 4-tetrahydro-pyrido[4,3-b]indol-5-yl)-acetic acid are disclosed by Kyle F. et *al.* in two patent specifications i.e. in US 5,817,756 and WO 95/07294, respectively.

Furthermore, a certain oral bioavailability of Ramatroban and its ability to inhibit prostaglandin D2-induced eosinophil migration *in vitro* has been reported in *Journal of Pharmacology and Experimental Therapeutics*, **305(1)**, p.347-352 (2003).

The present invention relates to the use of 2-sulfanyl-benzoimidazol-1-yl-acetic acids of the general Formula I



I

wherein

R^1, R^2, R^3 and R^4 each independently represent hydrogen; alkyl; haloalkyl; halogen; nitro; cyano; formyl; methylsulfonyl; or methylcarbonyl;

n is 0 or an integer from 1 to 10;

r is 0 or the integer 1, preferably 0;

R^5, R^6 and R^7 each independently represent hydrogen; alkyl; alkenyl; cycloalkyl; aryl; aryloxy; alkylcarbonyl; cycloalkylcarbonyl; alkoxycarbonyl, arylcarbonyl; arylalkylcarbonyl; N-alkyl-N-aryl-carbamoyl; N-alkyl-N-arylalkyl-carbamoyl; N-arylalkyl-N-aryl-carbamoyl; heterocyclyl (especially furanyl, oxazolyl or pyridinyl, all substituted by alkoxycarbonyl and optionally an additional halogen); heterocyclyloxy (especially 1-ethyloxycarbonyl-indazol-3-yl-oxy); heterocyclylcarbonyl (especially 3,4-dihydro-2H-quinolin-1-yl-carbonyl); or an amino of Formula NR^8R^9; or two of R^5-R^7 together with the carbon atom to which they are attached form cycloalkyl or saturated heterocyclyl;

R^8 represents hydrogen or R^9;

R^9 independently from R^8 represents cycloalkyl; cycloalkylalkyl; aryl; cycloalkylarylalkyl; arylalkyl; (diaryl)-alkyl; alkylcarbonyl; alkenylcarbonyl; cycloalkylcarbonyl; cycloalkylalkylcarbonyl; alkoxycarbonyl; alkoxydicarbonyl; arylcarbonyl; arylalkylcarbonyl; arylalkenylcarbonyl; (diaryl)-alkylcarbonyl; cycloalkylarylalkylcarbonyl; heterocyclylcarbonyl, especially furanylcarbonyl or pyridinylcarbonyl; alkylcarbamoyl; arylcarbamoyl; arylalkylcarbamoyl; alkylsulfonyl; arylsulfonyl; arylalkylsulfonyl; or

R^8 and R^9, together with the nitrogen atom to which they are attached, form a heterocyclyl group;

R^{11} is hydrogen or methyl, preferably hydrogen;

and optically pure enantiomers, mixtures of enantiomers, racemates, optically pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates, meso forms, geometric isomers, and prodrugs of compounds in which a prodrug forming group is present, as well as solvates and pharmaceutically acceptable salts of such compounds, and morphological forms;

for the manufacture of medicaments for the control of disorders responding to CRTH2 receptor antagonist treatment.

The present invention also relates to the use of a compound of Formula I as defined above, wherein R^1, R^2, R^3 and R^4 each independently represent hydrogen, alkyl, haloalkyl, halogen, nitro, cyano or formyl; r is 0; and R^{11} is hydrogen.

The present invention relates to compounds of Formula I as defined above, with the exception of:

(2-octylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-butylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-propylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-ethylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-methylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-isopropylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-*sec*-butylsulfanyl-benzoimidazol-1-yl)-acetic acid;

2-[(2-methylpropyl)thio]-1*H*-benzimidazole-1-acetic acid;

(2-allylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-cyclohexylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-benzylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-phenethylsulfanyl-benzoimidazol-1-yl)-acetic acid;

[2-(naphthalen-1-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[2-(4-*tert*-butyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-propoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-ethoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(3,4-dimethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(3-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(naphthalen-2-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-methoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-butoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[2-(4-ethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-isopropyl-4-methyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(naphthalen-1-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2,6-dimethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-isopropoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-fluoro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-methoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid; and

{2-[3-methyl-4-(2-morpholin-4-yl-ethylsulfanyl)-pyridin-2-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid (US patent 5,504,082).

A subgroup of novel compounds falling under Formula I are those wherein

R^5 represents hydrogen;

R^6 represents hydrogen; alkyl; or alkoxycarbonyl; and

R^7 represents alkoxycarbonyl; N-alkyl-N-arylalkyl-carbamoyl; N-alkyl-N-aryl-carbamoyl; alkylcarbonyl; N-arylalkyl-N-aryl-carbamoyl; arylalkylcarbonyl; arylcarbonyl; cycloalkylcarbonyl; heterocyclylcarbonyl; heterocyclyloxy; an amino of Formula NR^8R^9; aryl substituted with one or two of alkoxy, alkylcarbonyl, and alkoxycarbonyl and optionally an additional halogen; or heterocyclyl substituted with alkylcarbonyl, cycloalkylcarbonyl, alkoxycarbonyl, arylcarbonyl, arylalkylcarbonyl, (diaryl)alkyl carbonyl or heterocyclylcarbonyl and optionally an additional halogen; or

R^6 represents alkyl or alkoxycarbonyl and R^7 represents aryl; or

R^6 and R^7 together with the carbon atom to which they are attached form cycloalkyl or saturated heterocyclyl.

The present invention especially relates to compounds of Formula I, wherein
R^1, R^2, R^3 and R^4 each independently represent hydrogen; alkyl; haloalkyl; halogen; nitro; cyano; formyl; methylsulfonyl; or methylcarbonyl;
n is 0 or an integer from 1 to 5;
r is 0 or the integer 1;
R^5, R^6 and R^7 each independently represent hydrogen; alkyl; alkenyl; cycloalkyl, especially cyclohexyl; aryl, wherein aryl is especially phenyl, optionally mono- or di-substituted wherein the substitutents are independently selected from the group consisting of hydroxy-alkyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, halo, alkylcarbonyl, phenyl, 2,3-dihydro-indole-1-carbonyl, alkylcarbamoyl, morpholine-4-carbonyl, benzylcarbamoyl, N,N-dialkylcarbamoyl, N-alkyl-N-benzyl-carbamoyl, hydroxyalkoxy and benzoyl, or wherein aryl is especially 3-oxo-indan-5-yl or 8-oxo-5,6,7,8-tetrahydro-naphthalen-2-yl, both substituted by alkoxy; aryloxy, wherein aryl is especially naphthyl or phenyl, wherein phenyl is optionally substituted by halo; alkoxycarbonyl; arylcarbonyl, wherein aryl is especially phenyl; N-alkyl-N-aryl-carbamoyl, wherein aryl is especially phenyl; N-alkyl-N-arylalkyl-carbamoyl, wherein aryl is especially phenyl; N-arylalkyl-N-aryl-carbamoyl, wherein aryl is especially phenyl; heterocyclyl, especially furanyl, oxazolyl or pyridinyl, all substituted by alkoxycarbonyl and optionally an additional halogen; heterocyclyloxy, especially 1-alkoxycarbonyl-indazol-3-yl-oxy; heterocyclylcarbonyl, especially 3,4-dihydro-2H-quinolin-1-yl-carbonyl; or an amino of Formula NR^8R^9; or two of R^5-R^7 together with the carbon atom to which they are attached form cycloalkyl, especially cyclopentyl, cyclohexyl or bicyclo[4.2.0]octa-1,3,5-trien-7-yl; or or two of R^5-R^7 together with the carbon atom to which they are attached form saturated heterocyclyl, especially a 5- or 6-membered nitrogen containing saturated heterocyclyl containing one nitrogen ring atom (preferably piperidin-3-yl or pyrrolidin-3-yl), wherein this nitrogen ring atom contains a substituent R^{10}, wherein R^{10} is as defined hereinbelow;
R^8 represents hydrogen or R^9;

R^9 independently from R^8 represents cycloalkyl, especially cyclopropyl or cyclohexyl; cycloalkylalkyl, wherein cycloalkyl is especially cyclohexyl; aryl, especially phenyl which is optionally substituted by alkoxycarbonyl or piperidinyl; arylalkyl, wherein aryl is especially phenyl; (diaryl)-alkyl, wherein aryl is especially phenyl; alkylcarbonyl; cycloalkylcarbonyl, wherein cycloalkyl is especially cyclopropyl or cyclohexyl; cycloalkylalkylcarbonyl, wherein cycloalkyl is especially cyclopentyl; alkoxycarbonyl; alkoxydicarbonyl; arylcarbonyl, wherein aryl is especially naphthyl or phenyl, wherein phenyl is optionally substituted by alkoxy, halogen or phenyl; arylalkylcarbonyl, wherein aryl is especially phenyl, and wherein the alkyl moiety may optionally be substituted by cyclohexyl; arylalkenylcarbonyl, wherein aryl is especially phenyl; (diaryl)-alkylcarbonyl, wherein aryl is especially phenyl; heterocyclylcarbonyl, wherein heterocyclyl is especially furanyl or pyridinyl; alkylcarbamoyl; arylcarbamoyl, wherein aryl is especially phenyl; arylalkylcarbamoyl, wherein aryl is especially phenyl; alkylsulfonyl; arylsulfonyl, wherein aryl is especially phenyl; arylalkylsulfonyl, wherein aryl is especially phenyl; or

R^8 and R^9, together with the nitrogen atom to which they are attached, form a heterocyclyl group, especially1,3-dioxo-1,3-dihydro-isoindol-2-yl, 2,3-dihydro-1-ethyloxycarbonyl-3-oxo-indazol-2-yl, 1-oxo-1,3-dihydro-isoindol-2-yl, 2-oxo-2,3-dihydro-benzoimidazol-1-yl, 1-oxo-1H-phthalazin-2-yl, 2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl, or 1,1,3-trioxo-1,3-dihydro-1λ^6-benzo[d]isothiazol-2-yl; and

R^{11} is hydrogen or methyl;

with the exception of the following compounds:

(2-octylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-butylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-propylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-ethylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-methylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-isopropylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-*sec*-butylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-isobutylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-allylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-cyclohexylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-benzylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-phenethylsulfanyl-benzoimidazol-1-yl)-acetic acid;

[2-(naphthalen-1-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[2-(4-*tert*-butyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-propoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-ethoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(3,4-dimethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(3-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(naphthalen-2-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-methoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-butoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[2-(4-ethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-isopropyl-4-methyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(naphthalen-1-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2,6-Dimethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-isopropoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-fluoro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-methoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid; and

{2-[3-methyl-4-(2-morpholin-4-yl-ethylsulfanyl)-pyridin-2-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid.

In the above compounds of Formula I, aryl groups (preferably phenyl or naphthyl, especially phenyl) present as R^5-R^8, especially R^5-R^9, alone or in combination, are preferably unsubstituted or mono- or di-substituted with substituents independently selected from lower alkyl; lower alkoxy; halogen; cyano; lower alkoxycarbonyl; lower alkylcarbonyl; aryl, especially phenyl; aryl-lower alkyl; cycloalkyl; and heterocyclyl, such as especially piperidinyl.

In another embodiment, aryl groups (preferably phenyl, naphthyl, 3-oxo-indan-5-yl, or 8-oxo-5,6,7,8-tetrahydro-naphthalen-2-yl, especially phenyl) present as R^5-R^9, alone or in combination, are preferably unsubstituted or mono- or di-substituted with substituents independently selected from lower alkyl; hydroxy-lower alkyl; lower alkoxy; lower alkoxy-lower alkyl; halogen; cyano; lower alkoxycarbonyl; lower alkylcarbonyl; aryl, especially phenyl; aryl-lower alkyl; cycloalkyl; 2,3-dihydro-indole-1-carbonyl; lower alkylcarbamoyl; morpholine-4-carbonyl; aryl-lower alkylcarbamoyl, especially benzylcarbamoyl; N,N-di-lower alkylcarbamoyl; N-lower alkyl-N-aryl-lower alkyl-carbamoyl, especially N-lower alkyl-N-benzyl-carbamoyl; hydroxy-lower alkoxy; arylcarbonyl, especially benzoyl; and heterocyclyl, such as especially piperidinyl. Preferably the substitutents are independently selected from hydroxy-lower alkyl; lower alkoxy; lower alkoxy-lower alkyl; halogen; lower alkoxycarbonyl; lower alkylcarbonyl; phenyl; 2,3-dihydro-indole-1-carbonyl; lower alkylcarbamoyl; morpholine-4-carbonyl; benzylcarbamoyl; N,N-di-lower alkylcarbamoyl; N-lower alkyl-N-benzyl-carbamoyl; hydroxy-lower alkoxy; benzoyl; and piperidinyl.

Where two of R^5-R^7 together with the carbon atom, to which they are attached, form saturated heterocyclyl (preferably piperidinyl or pyrrolidinyl), this group may contain one nitrogen atom which is substituted with R^{10}, wherein R^{10} represents alkylcarbamoyl; alkylcarbonyl; alkoxycarbonyl; alkylsulfonyl; arylalkylcarbamoyl; arylalkylcarbonyl; arylalkoxycarbonyl; arylalkylsulfonyl; arylcarbamoyl; arylcarbonyl; aryloxycarbonyl; arylsulfonyl; cycloalkylcarbamoyl; cycloalkylcarbonyl; cycloalkyloxycarbonyl; cycloalkylsulfonyl; heterocyclylcarbamoyl; heterocyclylcarbonyl; heterocyclyloxycarbonyl; or heterocyclylsulfonyl.

In another preferred embodiment of the invention R^5-R^7 together with the carbon atom, to which they are attached, form saturated heterocyclyl (preferably piperidinyl or pyrrolidinyl), this group may contain one nitrogen atom which is substituted with R^{10}, wherein R^{10} represents alkylcarbamoyl; alkylcarbonyl; alkoxycarbonyl; alkylsulfonyl; arylalkylcarbamoyl; arylalkylcarbonyl; arylalkoxycarbonyl; arylalkylsulfonyl; arylcarbamoyl; arylcarbonyl; (diaryl)-alkylcarbonyl; aryloxycarbonyl; arylsulfonyl; arylalkenylsulfonyl; cycloalkylcarbamoyl; cycloalkylalkylcarbonyl;

cycloalkylcarbonyl; cycloalkyloxycarbonyl; cycloalkylsulfonyl; heterocyclylcarbamoyl; heterocyclylcarbonyl; heterocyclyloxycarbonyl; or heterocyclylsulfonyl. Preferably R^{10} represents alkylcarbonyl; alkylsulfonyl; arylalkylcarbonyl, wherein aryl is especially phenyl; arylalkoxycarbonyl, wherein aryl is especially phenyl; arylalkylsulfonyl, wherein aryl is especially phenyl; arylcarbonyl, wherein aryl is especially phenyl substituted by alkoxy or halo or wherein aryl is naphthyl; (diaryl)-alkylcarbonyl, wherein aryl is especially phenyl; arylsulfonyl, wherein aryl is especially phenyl substituted by alkyl or alkoxy or wherein aryl is naphthyl; arylalkenylsulfonyl, wherein aryl is especially phenyl; cycloalkylalkylcarbonyl, wherein cycloalkyl is especially cyclopentyl; cycloalkylcarbonyl, wherein cycloalkyl is especially cyclohexyl; heterocyclylcarbonyl, wherein heterocyclyl is especially furyl; or heterocyclylsulfonyl, wherein heterocyclyl is especially thienyl.

Preferably, in a compound of Formula I substituents R^1, R^2, R^3 and R^4 each independently represent hydrogen; methyl; trifluoromethyl; fluoro, chloro, bromo; nitro; cyano; formyl; methylsulfonyl; or methylcarbonyl.

Also preferably, in a compound of Formula I substituents R^1, R^2, R^3 and R^4 each independently represent hydrogen; methyl; trifluoromethyl; fluoro, chloro, bromo; nitro; cyano; or formyl.

In the subgroups (aspects) enumerated below R^1-R^4 are as above or as in Formula I.

In a preferred aspect, n in Formula I is 1 or 2; R^5 and R^6 each represent hydrogen; R^7 represents an amino of Formula NR^8R^9;
R^8 represents hydrogen or R^9; and
R^9 independently from R^8 represents cycloalkyl; cycloalkylalkyl; aryl; arylalkyl; (diaryl)-alkyl; alkylcarbonyl; cycloalkylcarbonyl; cycloalkylalkylcarbonyl; alkoxycarbonyl; alkoxydicarbonyl; arylcarbonyl; arylalkylcarbonyl; arylalkenylcarbonyl; (diaryl)-alkylcarbonyl; heterocyclylcarbonyl; alkylcarbamoyl; arylcarbamoyl; arylalkylcarbamoyl; alkylsulfonyl; arylsulfonyl; arylalkylsulfonyl,

wherein aryl groups present as R^8 and/or R^9, alone or in combination with other groups, preferably represent phenyl or naphthyl, especially phenyl, wherein the phenyl is optionally substituted by alkoxy, alkoxycarbonyl, halogen, phenyl or piperidinyl; or R^8 and R^9, together with the nitrogen atom to which they are attached, form a heterocyclyl group, wherein said heterocyclyl group preferably represents 1,3-dioxo-1,3-dihydro-isoindol-2-yl, 2,3-dihydro-1-ethyloxycarbonyl-3-oxo-indazol-2-yl, 1-oxo-1,3-dihydro-isoindol-2-yl, 2-oxo-2,3-dihydro-benzoimidazol-1-yl, 1-oxo-1H-phthalazin-2-yl, 2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl, or 1,1,3-trioxo-1,3-dihydro-1λ^6-benzo[d]isothiazol-2-yl.

In another preferred embodiment, n in Formula I is 2 or 3, especially 1 or 2; R^5 and R^6 each represent hydrogen; R^7 represents an amino of Formula NR^8R^9;

R^8 represents hydrogen; and

R^9 represents cycloalkyl; aryl; arylalkyl; (diaryl)-alkyl; alkylcarbonyl; cycloalkyl-alkylcarbonyl; cycloalkylcarbonyl; alkenylcarbonyl; alkoxycarbonyl; alkoxydicarbonyl; arylcarbonyl; arylalkylcarbonyl; (diaryl)-alkylcarbonyl; heterocyclylcarbonyl; alkylcarbamoyl; arylcarbamoyl; arylalkylcarbamoyl; alkylsulfonyl; arylsulfonyl; arylalkylsulfonyl; or

R^8 represents cycloalkyl; arylalkyl; aryl; alkoxycarbonyl; and

R^9 represents cycloalkyl; cyclylalkyl-alkyl; aryl; arylalkyl; (diaryl)-alkyl; cycloalkyl-alkylcarbonyl; alkylcarbonyl; arylalkylcarbonyl; (diaryl)-alkylcarbonyl; alkylcarbamoyl; arylcarbamoyl; arylalkylcarbamoyl; alkylsulfonyl; arylsulfonyl; arylalkylsulfonyl; or

R^8 and R^9, together with the nitrogen atom to which they are attached, form a phthalazinyl; isoindolyl; benzoimidazolyl; indazolyl; quinazolinyl; or benzoisothiazolyl ring system, such as especially 1,3-dioxo-1,3-dihydro-isoindol-2-yl, 2,3-dihydro-1-ethyloxycarbonyl-3-oxo-indazol-2-yl, 1-oxo-1,3-dihydro-isoindol-2-yl, 2-oxo-2,3-dihydro-benzoimidazol-1-yl, 1-oxo-1H-phthalazin-2-yl, 2,4-dioxo-1,4-dihydro-2H-quinazolin-3-yl, or 1,1,3-trioxo-1,3-dihydro-1λ^6-benzo[d]isothiazol-2-yl.

In a preferred aspect of the invention, R^8 represents hydrogen; and

R^9 represents particularly 3-phenyl-acryloyl; butoxycarbonyl, *tert*-butoxycarbonyl; ethoxydicarbonyl; propylcarbamoyl; 2,2-dimethyl-propionyl; 3,3-dimethyl-butyryl, 3-octanoyl, pentanoyl; butane-1-sulfonyl; 4-piperidin-1-yl-phenyl, phenyl; 2,2-diphenyl-ethyl, 3-benzyl; 2-cyclohexyl-2-phenyl-acetyl, 3,3-diphenyl-propionyl, 3-phenyl-propionyl, diphenylacetyl, phenylacetyl; phenylmethanesulfonyl; phenylcarbamoyl; 4-bromo-benzoyl, 4-methoxy-benzoyl, benzoyl, biphenyl-4-carbonyl, naphthalene-1-carbonyl, benzenesulfonyl; cyclohexanecarbonyl, cyclopropanecarbonyl, 3-cyclopentyl-propionyl; furan-2-carbonyl, or pyridine-3-carbonyl; or

R^8 represents particularly butoxycarbonyl, *tert*-butoxycarbonyl; 4-carboethoxyphenyl, 4-piperidin-1-yl-phenyl, phenyl; benzyl, 2,2-diphenyl-ethyl, phenethyl; cyclopropyl; and

R^9 represents particularly propylcarbamoyl; pentanoyl; butane-1-sulfonyl; 4-piperidin-1-yl-phenyl, phenyl; benzyl, phenethyl, 2,2-diphenyl-ethyl; benzylcarbamoyl; 2-cyclohexyl-2-phenyl-acetyl, 2-phenylacetyl, 3,3-diphenyl-propionyl, diphenylacetyl, phenylmethanesulfonyl; phenylcarbamoyl; benzenesulfonyl; cyclohexyl, cyclopropyl; or cyclohexylmethyl; or

R^8 and R^9, together with the nitrogen atom to which they are attached, represent particularly 1-oxo-1*H*-phthalazin-2-yl; 1-oxo-1,3-dihydro-isoindol-2-yl; 2-oxo-2,3-dihydro-benzoimidazol-1-yl; 1-ethoxycarbonyl-3-oxo-2,3-dihydro-indazole-2-yl; 2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-yl; or 1,3-dioxo-1,3-dihydro-isoindol-2-yl; 1,1,3-trioxo-1,3-dihydro-1λ^6-benzo[d]isothiazol-2-yl.

In another preferred aspect, n in Formula I is 0;

R^5 and R^6 each represent hydrogen;

R^7 represents phenyl; furanyl, oxazolyl, pyridinyl or thiazolyl, all substituted with one or two of alkoxy, alkylcarbonyl, and alkoxycarbonyl and optionally an additional halogen.

In this aspect, R^7 represents particularly halogen or alkoxy substituted (alkoxycarbonyl)phenyl; (alkylcarbonyl)phenyl; (alkoxycarbonyl)furanyl, or (alkoxycarbonyl)pyridinyl;

more particularly halogen or alkoxy substituted 3-(alkoxycarbonyl)phenyl; 3-(alkylcarbonyl)phenyl; 5-(alkoxycarbonyl)furan-2-yl, 5-(alkoxycarbonyl)pyridin-3-yl; or 4-(alkoxycarbonyl)pyridin-2-yl;

most particularly, R^7 represents 3-(methoxycarbonyl)phenyl; 2-bromo-3-(methoxycarbonyl)phenyl, 4-bromo-3-(methoxycarbonyl)phenyl, 5-bromo-3-(methoxycarbonyl)phenyl, 2-bromo-5-(methoxycarbonyl)phenyl, 2-methoxy-5-(methoxycarbonyl)phenyl; 3-acetyl-phenyl, 5-acetyl-2-methoxy-phenyl; 5-(methoxycarbonyl)pyridine-3-yl, 6-chloro-4-(methoxycarbonyl)pyridine-2-yl; or 5-(ethoxycarbonyl)furan-2-yl; most preferred 5-acetyl-2-methoxy-phenyl.

A preferred embodiment of the invention n in Formula I is 0; R^5 and R^6 each represent hydrogen; and R^7 represents phenyl, optionally mono- or di-substituted wherein the substitutents are independently selected from the group consisting of hydroxy-alkyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, halo, alkylcarbonyl, phenyl, 2,3-dihydro-indole-1-carbonyl, alkylcarbamoyl, morpholine-4-carbonyl, benzylcarbamoyl, N,N-dialkylcarbamoyl, N-alkyl-N-benzyl-carbamoyl, hydroxyalkoxy and benzoyl; or R^7 represents 3-oxo-indan-5-yl or 8-oxo-5,6,7,8-tetrahydro-naphthalen-2-yl, both substituted by alkoxy.

In a more preferred aspect, n in Formula I is 1;

R^5 represents hydrogen;

R^6 and R^7 together with the carbon atom to which they are attached form a 5- or 6-membered nitrogen containing saturated heterocyclyl containing one nitrogen ring atom, wherein this nitrogen ring atom contains a substituent R^{10}, wherein R^{10} is as defined hereinabove;

most preferred in this aspect, R^6 and R^7 form a piperidinyl, particularly a piperidin-3-yl ring; and

R^{10} represents particularly acetyl, butyryl, heptanoyl; 1-phenylacetyl, 3-phenyl-propionyl, diphenylacetyl; naphthalene-1-carbonyl, 2-methoxy-benzoyl, 3-chloro-benzoyl, 4-bromo-benzoyl; 1-cyclohexanecarbonyl, 3-cyclopentyl-propionyl; or furan-2-carbonyl, most preferred butyryl.

Most preferred novel compounds of the present invention include:
{2-[3-(butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-5-nitro-benzoimidazol-1-yl}-acetic acid;
rac [2-(3-{(2-cyclohexyl-2-phenyl-acetyl)-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid; and
[2-(5-acetyl-2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid.

The present invention also especially relates to a compound selected from:
[2-(5-acetyl-2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
rac [2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[3-(butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[3-(pentanoyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
and pharmaceutically acceptable salts, especially the sodium salt, of these compounds.

Particularly preferred novel compounds of the present invention include:
{2-[3-(butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid and its sodium salt;
{2-[3-(pentanoyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
(2-{3-[(2,2-diphenyl-ethyl)-pentanoyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
[2-(3-methoxycarbonyl-benzylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid;
rac {2-[1-(4-bromo-benzoyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
rac [2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[(6-methoxy-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
[5-fluoro-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-fluoro regioisomer;
{2-[(6-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
[2-(3-{butyloxycarbonyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[5-cyano-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-cyano regioisomer;

[2-(4-ethyloxycarbonyl-butylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid;

[2-(3-{diphenylacetyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(3-{[(4-ethyloxycarbonyl)-phenyl]-pentanoyl-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

rac {2-[1-(furan-2-carbonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(benzyl-butoxycarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(3-phenyl-propionyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[(4-ethyloxycarbonylphenyl)-(phenylacetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(benzyl-pentanoyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(cyclopropyl-diphenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid; and

[2-(3-{diphenylpropionyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid.

Preferred novel compounds of the present invention include:

rac [2-(1-methyl-2-oxo-2-phenyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(3-methoxycarbonyl-benzylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetic acid and its 6-trifluoromethyl regioisomer;

[2-(3,3-diphenyl-propylsulfanyl)-6-nitro-benzoimidazol-1-yl]-acetic acid;

(2-benzylsulfanyl-5-nitro-benzoimidazol-1-yl)-acetic acid and its 6-nitro isomer;

{2-[3-(1-phenethyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(3-chloro-benzoyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-5-nitro-benzoimidazol-1-yl}-acetic acid;

{2-[3-(1,1,3-trioxo-1,3-dihydro-1λ^6-benzo[d]isothiazol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[(2,2-diphenyl-ethyl)-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

(2-{3-[cyclopropyl-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

rac (2-{3-[(2-cyclohexyl-2-phenyl-acetyl)-cyclopropyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

(2-{3-[diphenylacetyl-(2,2-diphenyl-ethyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

rac [2-(1-heptanoyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[3-(3,3-diphenyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[(butane-1-sulfonyl)-phenethyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(benzyl-(phenylmethanesulfonyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[(2,2-diphenyl-ethyl)-(phenylacetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(benzenesulfonyl-cyclopropyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(phenethyl-(phenylmethanesulfonyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(3,3-diphenyl-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[3-(phenethyl-(phenylacetyl)amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(diphenylacetyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{[(2-chloro-4-methyloxycarbonyl)-pyridin-6-yl]-methyl-sulfanyl}-benzoimidazol-1-yl)-acetic acid;

rac [2-(bicyclo[4.2.0]octa-1,3,5-trien-7-ylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(3-acetyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[5-fluoro-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-fluoro regioisomer;

[2-(3-phenylmethanesulfonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(4-ethyloxycarbonyl-butylsulfanyl)-6-nitro-benzoimidazol-1-yl]-acetic acid;

{2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-6-nitro-benzoimidazol-1-yl}-acetic acid;

(2-{3-[phenylmethanesulfonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

[2-(4-ethyloxycarbonyl-butylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid and its 6-fluoro regioisomer;

[2-(3-diphenylacetylamino-propylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid;

{2-[3-(cyclopropyl-(phenylmethanesulfonyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[(5-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{5-nitro-2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(3,3-diphenyl-propylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid;

{2-[3-(2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(benzyl-(phenylacetyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[(2,2-diphenyl-ethyl)-(phenylmethanesulfonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

rac [2-(1-acetyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

(2-{3-[benzyl-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(cyclopropyl-(phenylacetyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac [2-(1-methyloxycarbonyl-1-phenyl-methylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[3-(butoxycarbonyl-cyclohexyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(3-diphenylacetylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[3-(1,3-diphenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
(2-benzylsulfanyl-6-nitro-benzoimidazol-1-yl)-acetic acid;
rac [2-(1-diphenylacetyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[3-(cyclopropyl-pentanoyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
(2-{3-[benzenesulfonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
{2-[3-(benzyl-diphenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[3-(*tert*-butoxycarbonyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
[2-(3-phenyl-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
[2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
[2-(3-benzenesulfonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[3-(1-benzyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
(2-{3-[1-(2,2-diphenyl-ethyl)-3-propyl-ureido]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
[2-(4-ethyloxycarbonyl-butylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetic acid and its 6-trifluoromethyl regioisomer;
[5-cyano-2-(4-ethyloxycarbonyl-butylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-cyano regioisomer;
[2-(5-ethyloxycarbonyl-pentylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
(2-{3-[(3,3-diphenyl-propionyl)-phenyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
{2-[3-(butoxycarbonyl-(cyclohexylmethyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
(2-{3-[*tert*-butoxycarbonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
(2-{3-[phenylacetyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
{2-[3-(2,3-dihydro-1-ethyloxycarbonyl-3-oxo-indazol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(3-cyclopentyl-propionyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[*tert*-butoxycarbonyl-(2,2-diphenyl-ethyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(benzenesulfonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid; and

{2-[5-(3,4-dihydro-2*H*-quinolin-1-yl)-5-oxo-pentylsulfanyl]-benzoimidazol-1-yl}-acetic acid.

Further preferred novel compounds of the present invention include:

{2-[3-(phenyl-phenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[(3,3-diphenyl-propionyl)-phenethyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

rac [2-(1-cyclohexanecarbonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[3-(3-benzyl-1-phenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(butane-1-sulfonylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(benzyl-*tert*-butoxycarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(diphenylacetyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac [2-(1-phenylacetyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(2-cyclohexyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(3-phenoxy-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

(2-{3-[(butane-1-sulfonyl)-cyclopropyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

[5-cyano-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-cyano regioisomer;

{2-[3-(benzenesulfonyl-benzyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(benzenesulfonyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-hexylsulfanyl-benzoimidazol-1-yl)-acetic acid;

{2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-5-methyl-benzoimidazol-1-yl}-acetic acid and its 6-methyl regioisomer;

rac (2-{3-[benzyl-(2-cyclohexyl-2-phenyl-acetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[(4-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(pentanoyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(2-methoxy-benzoyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac [2-(1-phenyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(4-ethyloxycarbonyl-butylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[3-(3-phenyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[4-(benzyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[(2-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(3-phenyl-ureido)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(3-phenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[4-(butyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(4-bromo-benzoylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(1-oxo-1*H*-phthalazin-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(*tert*-butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[pentanoyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

(2-{3-[(3,3-diphenyl-propionyl)-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

rac {2-[1-(naphthalene-1-carbonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[5-nitro-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(3-benzoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[3-(2,2-diphenyl-ethylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
[2-(3-phenylacetylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
[2-(4-phenoxy-butylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[3-(cyclohexanecarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
[2-(3-phenylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
(2-{3-[(naphthalene-1-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
[2-(2-diphenylacetylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
rac (2-{3-[(2-cyclohexyl-2-phenyl-acetyl)-phenyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
{2-[3-(1,2-dioxo-2-ethyloxy-ethylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-4-methyl-benzoimidazol-1-yl}-acetic acid and its 8-methyl regioisomer;
{2-[3-(*tert*-butoxycarbonyl-cyclopropyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[(2-methyloxycarbonyl-furan-5-yl)-methylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
(2-{3-[diphenylacetyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
{2-[4-(methyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[4-(benzyl-methyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[3-(4-methoxy-benzoylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[3-(cyclopropanecarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{5-chloro-2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid and its 6-chloro regioisomer;
(2-{3-[(biphenyl-4-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
{2-[3-(3-cyclopentyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
[2-(3-octanoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(3-phenyl-acryloylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[(5-methyloxycarbonyl-pyridin-3-yl)-methylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[6-iodo-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

rac. {2-[3-(2-cyclohexyl-2-phenyl-acetylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(4-piperidin-1-yl-phenylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(3-*tert*-butoxycarbonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(2-butoxycarbonylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

(2-{3-[(pyridine-3-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(3,3-dimethyl-butyrylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[1-(4-piperidin-1-yl-phenyl)-3-propyl-ureido]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

(2-cyclopentylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-but-3-enylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-{3-[(furan-2-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(2,2-dimethyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(2-*tert*-butoxycarbonylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(2-phenylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

(2-{3-[(1-ethyloxycarbonyl-indazol-3-yl)-oxy]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

[2-(3-pentanoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(3-ethyloxycarbonyl-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[3-(1-cyclopropyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid; and [2-(3-benzylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid.

Particulary preferred novel compounds of the present invention include:

rac {2-[1-(3,4-dichloro-benzenesulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(3-phenyl-acryloyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-5,6-dimethyl-benzoimidazol-1-yl]-acetic acid;

[2-(5-methyloxycarbonyl-benzylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetic acid;

[2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetic acid;

[2-((R)-1-butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5,6-difluoro-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

rac [2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

rac {5-fluoro-2-[1-(furan-2-carbonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(4-bromo-benzoyl)-piperidin-3-ylmethylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-methanesulfonyl-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-6-fluoro-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-4-fluoro-benzoimidazol-1-yl]-acetic acid;

[5-acetyl-2-(5-acetyl-2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-formyl-benzoimidazol-1-yl]-acetic acid;

rac 2-[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-propionic acid;

[2-(5-butylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

[2-(5-benzylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

{2-[5-(2,3-dihydro-indole-1-carbonyl)-2-methoxy-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid;

[2-(5-diethylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid;

rac {2-[1-(4-bromo-benzoyl)-pyrrolidin-3-ylmethylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid;

rac {5-fluoro-2-[1-(furan-2-carbonyl)-pyrrolidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {5-fluoro-2-[1-(2-phenyl-ethenesulfonyl)-pyrrolidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(5-acetyl-2-butoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

{2-[5-acetyl-2-(3-hydroxy-propoxy)-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid;

[2-(5-benzoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

[5-fluoro-2-(6-methoxy-3-oxo-indan-5-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-ethoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-propoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid; and

rac [2-(5-acetyl-2-methoxy-phenylmethanesulfinyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid.

Further preferred novel compounds of the present invention include:

[2-(1-butyryl-piperidin-4-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(3-isopropyloxycarbonyl-6-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

rac {2-[1-(propane-2-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac [2-(1-methanesulfonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

rac {2-[1-(thiophene-2-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(butane-1-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac [2-(1-phenylmethanesulfonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

rac {2-[1-(naphthalene-2-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(toluene-4-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(4-methoxy-benzenesulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(5-methyloxycarbonyl-benzylsulfanyl)-5,6-dimethyl-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5,6-dimethyl-benzoimidazol-1-yl]-acetic acid;

[2-(5-methyloxycarbonyl-benzylsulfanyl)-4,6-bis-trifluoromethyl-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-4,6-bis-trifluoromethyl-benzoimidazol-1-yl]-acetic acid;

[2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-4,6-bis-trifluoromethyl-benzoimidazol-1-yl]-acetic acid;

[2-(4-methyloxycarbonyl-oxazol-2-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-((S)-1-butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

rac {2-[5-(1-hydroxy-ethyl)-2-methoxy-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[2-methoxy-5-(1-methoxy-ethyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(3-methyloxycarbonyl-6-phenyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[5-(benzyl-ethyl-carbamoyl)-2-methoxy-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid;

{2-[2-methoxy-5-(morpholine-4-carbonyl)-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid;

rac [2-(1-butyryl-pyrrolidin-3-ylmethylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

rac [5-fluoro-2-(1-octanoyl-pyrrolidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

rac {5-fluoro-2-[1-(3-phenyl-propionyl)-pyrrolidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac [5-fluoro-2-(1-phenylacetyl-pyrrolidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

rac {2-[1-(butane-1-sulfonyl)-pyrrolidin-3-ylmethylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid;

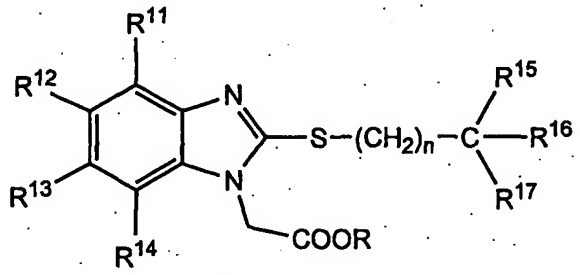
rac {5-fluoro-2-[1-(4-methoxy-benzenesulfonyl)-pyrrolidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[5-fluoro-2-(3-methoxy-8-oxo-5,6,7,8-tetrahydro-naphthalen-2-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

(S)-[5-fluoro-2-(1-benzyloxycarbonyl-azetidin-2-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid; and

[5-fluoro-2-(1-benzyloxycarbonyl-azetidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid

The present invention also relates to precursors of the general Formula II,



II

wherein R^1-R^7 and n are as in Formula I and R represents an alkyl group, preferably ethyl or *tert*-butyl, are novel with the exception of:

methyl [2-(5-trifluoromethyl-pyridin-2-ylsulfanyl)-benzoimidazol-1-yl]-acetate;

methyl [2-(4-chloro-benzylsulfanyl)-benzoimidazol-1-yl]-acetate;

methyl (2-benzylsulfanyl-benzoimidazol-1-yl)-acetate;

methyl [2-(5-nitro-pyridin-2-ylsulfanyl)-benzoimidazol-1-yl]-acetate;

methyl (2-methylsulfanyl-benzoimidazol-1-yl)-acetate;

ethyl (2-methylsulfanyl-benzoimidazol-1-yl)-acetate;

methyl (2-ethylsulfanyl-benzoimidazol-1-yl)-acetate;

ethyl [2-(1,3,7-trimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-purin-8-ylsulfanyl)-benzoimidazol-1-yl]-acetate;

ethyl {2-[3-methyl-4-(2-morpholin-4-yl-ethylsulfanyl)-pyridin-2-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate (US patent 5,504,082) and

methyl {2-[3-methyl-4-(2-morpholin-4-yl-ethylsulfanyl)-pyridin-2-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate (US patent 5,504,082).

These novel precursors also form part of the present invention. They include, *e.g.*:

tert-butyl [2-(2-cyclohexyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acetate;

tert-butyl (2-hexylsulfanyl-benzoimidazol-1-yl)-acetate;

tert-butyl (2-pentylsulfanyl-benzoimidazol-1-yl)-acetate;

tert-butyl (2-but-3-enylsulfanyl-benzoimidazol-1-yl)-acetate;

tert-butyl (2-butylsulfanyl-benzoimidazol-1-yl)-acetate;

rac *tert*-butyl [2-(1-phenyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl (2-cyclopentylsulfanyl-benzoimidazol-1-yl)-acetate;

rac *tert*-butyl [2-(1-methyloxycarbonyl-1-phenyl-methylsulfanyl)-benzoimidazol-1-yl]-acetate;

rac *tert*-butyl [2-(bicyclo[4.2.0]octa-1,3,5-trien-7-ylsulfanyl)-benzoimidazol-1-yl]-acetate;

rac *tert*-butyl [2-(1-methyl-2-oxo-2-phenyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl [2-(2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl (2-benzylsulfanyl-benzoimidazol-1-yl)-acetate;

tert-butyl (2-phenethylsulfanyl-benzoimidazol-1-yl)-acetate;

tert-butyl [2-(3-phenyl-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl [2-(3,3-diphenyl-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl {2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl [2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl {2-[2-(naphthalen-1-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[2-(naphthalen-2-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl [2-(4-phenoxy-butylsulfanyl)-benzoimidazol-1-yl]-acetate;
tert-butyl (2-{3-[(1-ethyloxycarbonyl-indazol-3-yl)-oxy]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;
tert-butyl [2-(4-phenoxy-butylsulfanyl)-benzoimidazol-1-yl]-acetate;
tert-butyl [2-(5-ethyloxycarbonyl-pentylsulfanyl)-benzoimidazol-1-yl]-acetate;
tert-butyl [2-(3-ethyloxycarbonyl-propylsulfanyl)-benzoimidazol-1-yl]-acetate;
tert-butyl [2-(4-ethyloxycarbonyl-butylsulfanyl)-benzoimidazol-1-yl]-acetate;
tert-butyl {2-[4-(benzyl-methyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[5-(3,4-dihydro-2*H*-quinolin-1-yl)-5-oxo-pentylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[4-(benzyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[4-(methyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[4-(butyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[3-(2,3-dihydro-1-ethyloxycarbonyl-3-oxo-indazol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[3-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[3-(1-oxo-1*H*-phthalazin-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[3-(2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[3-(1,1,3-trioxo-1,3-dihydro-1λ^6-benzo[d]isothiazol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl [2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl {2-[(5-methyloxycarbonyl-pyridin-3-yl)-methylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{[(2-chloro-4-methyloxycarbonyl)-pyridin-6-yl]-methyl-sulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[(2-methyloxycarbonyl-furan-5-yl)-methylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[(2-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-aceate;

tert-butyl {2-[(4-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[(5-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[(6-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[(6-methoxy-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl [2-(3-acetyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetate;

rac *tert*-butyl [2-(1-*tert*-butyloxycarbonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate;

rac *tert*-butyl [2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl {2-[3-(*tert*-Butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[*tert*-butoxycarbonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl [2-(3-{[(4-ethyloxycarbonyl)-phenyl]-*tert*-butyloxycarbonyl-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl {2-[3-(benzyl-*tert*-butoxycarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(*tert*-butoxycarbonyl-cyclopropyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(*tert*-butoxycarbonyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[*tert*-butoxycarbonyl-(2,2-diphenyl-ethyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(benzyl-butoxycarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(butoxycarbonyl-cyclohexyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(butoxycarbonyl-cyclohexylmethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(pentanoyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(diphenylacetyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(phenyl-phenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[(3,3-diphenyl-propionyl)-phenyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(benzenesulfonyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

rac *tert*-butyl (2-{3-[(2-cyclohexyl-2-phenyl-acetyl)-phenyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(1,3-diphenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(3-benzyl-1-phenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[pentanoyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[diphenylacetyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[phenylmethanesulfonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[phenylacetyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[(3,3-diphenyl-propionyl)-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[1-(4-piperidin-1-yl-phenyl)-3-propyl-ureido]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[benzenesulfonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl [2-(3-{[(4-ethyloxycarbonyl)-phenyl]-pentanoyl-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl [2-(3-{diphenylacetyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl (2-{3-[(4-ethyloxycarbonylphenyl)-(phenylacetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl [2-(3-{diphenylpropionyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

rac *tert*-butyl [2-(3-{(2-cyclohexyl-2-phenyl-acetyl)-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl {2-[3-(benzyl-pentanoyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(benzyl-diphenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(benzyl-phenylmethanesulfonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(benzyl-phenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[benzyl-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(1-benzyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(benzenesulfonyl-benzyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

rac *tert*-butyl(2-{3-[benzyl-(2-cyclohexyl-2-phenyl-acetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(cyclopropyl-pentanoyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[(butane-1-sulfonyl)-cyclopropyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(cyclopropyl-diphenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(cyclopropyl-phenylmethanesulfonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(cyclopropyl-phenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[cyclopropyl-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(1-cyclopropyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(benzenesulfonyl-cyclopropyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

rac *tert*-butyl (2-{3-[(2-cyclohexyl-2-phenyl-acetyl)-cyclopropyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(pentanoyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[(butane-1-sulfonyl)-phenethyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(diphenylacetyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(phenethyl-phenylmethanesulfonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(phenethyl-phenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[(3,3-diphenyl-propionyl)-phenethyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(1-phenethyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(benzenesulfonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl(2-{3-[(2,2-diphenyl-ethyl)-pentanoyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[diphenylacetyl-(2,2-diphenyl-ethyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[(2,2-diphenyl-ethyl)-phenylmethanesulfonyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[(2,2-diphenyl-ethyl)-phenylacetyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[(2,2-diphenyl-ethyl)-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[1-(2,2-diphenyl-ethyl)-3-propyl-ureido]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl [2-(3-{butyloxycarbonyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl [2-(3-*tert*-butoxycarbonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl [2-(3-pentanoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl {2-[3-(butane-1-sulfonylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl [2-(3-diphenylacetylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl [2-(3-phenylmethanesulfonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl [2-(3-phenylacetylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl {2-[3-(3,3-diphenyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl [2-(3-benzenesulfonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

rac *tert*-butyl {2-[3-(2-cyclohexyl-2-phenyl-acetylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(3-phenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl [2-(3-benzoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl {2-[3-(cyclohexanecarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(4-methoxy-benzoylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[(furan-2-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(cyclopropanecarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[(naphthalene-1-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl {2-[3-(3-cyclopentyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(2,2-dimethyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(3-phenyl-acryloylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl {2-[3-(3-phenyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-aceate;

tert-butyl {2-[3-(1,2-dioxo-2-ethyloxy-ethylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl (2-{3-[(biphenyl-4-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

tert-butyl (2-{3-[(pyridine-3-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate;

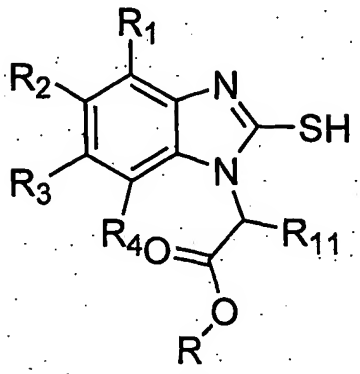
tert-butyl {2-[3-(3,3-dimethyl-butyrylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;

tert-butyl [2-(3-octanoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate;

tert-butyl {2-[3-(4-bromo-benzoylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate;
[3-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-phenethyl-ammonium chloride;
[3-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-(4-piperidin-1-yl-phenyl)-ammonium chloride;
[3-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-(4-ethoxycarbonyl-phenyl)-ammonium chloride;
benzyl-[3-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-ammonium chloride;
[3-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-cyclopropyl-ammonium chloride;
[3-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-phenyl-ammonium chloride;
[3-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-(2,2-diphenyl-ethyl)-ammonium chloride;
3-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl-ammonium chloride;
tert-butyl {2-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl [2-(2-*tert*-butoxycarbonylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetate;
tert-butyl [2-(2-butoxycarbonylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetate;
tert-butyl [2-(2-diphenylacetylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetate;
tert-butyl {2-[2-(3-phenyl-ureido)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate;
tert-butyl [6-iodo-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetate;
tert-butyl {5-chloro-2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate and its 6-chloro regioisomer;
tert-butyl {2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-4-methyl-benzoimidazol-1-yl}-acetate and its 8-methyl regioisomer;
tert-butyl (2-benzylsulfanyl-5-nitro-benzoimidazol-1-yl)-acetate;
tert-butyl [2-(3,3-diphenyl-propylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetate;
tert-butyl {5-nitro-2-[2-(4-chlorophenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate and its 6-nitro regioisomer;

tert-butyl-[5-nitro-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetate;
tert-butyl {2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-5-nitro-benzoimidazol-1-yl}-acetate;
tert-butyl [2-(4-ethyloxycarbonyl-butylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetate;
tert-butyl [2-(3-methoxycarbonyl-benzylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetate;
tert-butyl {2-[3-(butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-5-nitro-benzoimidazol-1-yl}-acetate;
tert-butyl {2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-5-methyl-benzoimidazol-1-yl}-acetate and its 6-methyl regioisomer;
tert-butyl [5-cyano-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetate and its 6-cyano regioisomer;
tert-butyl [5-cyano-2-(4-ethyloxycarbonyl-butylsulfanyl)-benzoimidazol-1-yl]-acetate and its 6-cyano regioisomer;
tert-butyl [5-cyano-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetate and its 6-cyano regioisomer;
tert-butyl [2-(4-ethyloxycarbonyl-butylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetate and its 6-trifluoromethyl regioisomer;
tert-butyl [2-(3-methoxycarbonyl-benzylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetate and its 6-trifluoromethyl regioisomer;
tert-butyl (2-benzylsulfanyl-6-nitro-benzoimidazol-1-yl)-acetate;
tert-butyl [2-(3,3-diphenyl-propylsulfanyl)-6-nitro-benzoimidazol-1-yl]-acetate;
tert-butyl [6-nitro-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetate and its 5-nitro regioisomer;
tert-butyl [2-(4-ethyloxycarbonyl-butylsulfanyl)-6-nitro-benzoimidazol-1-yl]-acetate;
tert-butyl {2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-6-nitro-benzoimidazol-1-yl}-acetate;
tert-butyl [5-fluoro-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetate and its 6-fluoro regioisomer;
tert-butyl [2-(4-ethyloxycarbonyl-butylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate and its 6-fluoro regioisomer; and
tert-butyl [5-fluoro-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetate and its 6-fluoro regioisomer.

The present invention also relates to novel intermediates of the general Formula



wherein R^1-R^4 and R^{11} are as defined for Formula I and R represents an alkyl group.

Such novel intermdediates include:
tert-butyl-(2-mercapto-benzoimidazol-1-yl)-acetate;
tert-butyl-(2-mercapto-5-nitro-benzoimidazol-1-yl)-acetate;
tert-butyl-(2-mercapto-6-nitro-benzoimidazol-1-yl)-acetate;
tert-butyl (5-formyl-2-mercapto-benzoimidazol-1-yl)-acetate;
tert-butyl (5,6-difluoro-2-mercapto-benzoimidazol-1-yl)-acetate;
tert-butyl (2-mercapto-5-methanesulfonyl-benzoimidazol-1-yl)-acetate;
tert-butyl (5-acetyl-2-mercapto-benzoimidazol-1-yl)-acetate;
tert-butyl (4-fuoro-2-mercapto-benzoimidazol-1-yl)-acetate;
tert-butyl (2-mercapto-5-trifluoromethyl-benzoimidazol-1-yl)-acetate;
tert-butyl (5-fluoro-2-mercapto-benzoimidazol-1-yl)-acetate;
methyl (6-fluoro-2-mercapto-benzoimidazol-1-yl)-acetate; and
rac ethyl 2-(5-fluoro-2-mercapto-benzoimidazol-1-yl)-propionate.

Unless explicitly stated otherwise, the general terms and names used hereinbefore and hereinafter preferably have within the context of this disclosure the following meanings:

Any reference to a compound of Formula I is to be understood as referring also to optically pure enantiomers, mixtures of enantiomers, racemates, optically pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures

of diastereoisomeric racemates, meso forms, geometric isomers, and prodrugs of compounds in which a prodrug forming group is present, as well as salts (especially pharmaceutically acceptable salts) and solvates (including hydrates) of such compounds, and morphological forms, as appropriate and expedient.

The term "alkyl", as used herein, alone or in any combination, refers to a saturated aliphatic group including a straight or branched hydrocarbon chain containing 1-8, preferably 1-4 carbon atoms. Representative examples of alkyl include, but are not limited to, methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *tert*-butyl, *iso*-butyl (or 2-methylpropyl), cyclopropylmethyl, *n*-pentyl, *iso*-pentyl, *iso*-amyl, *n*-amyl, *n*-hexyl, *n*-heptyl, *n*-octyl and the like. Less preferred, the alkyl group can be optionally substituted with one or more substituents, each independently selected from alkenyl, alkoxy, alkoxycarbonyl, alkylcarbonyl, alkylcarbonyloxy, alkylendioxy, alkylsulfinyl, alkylsulfonyl, alkylthio, alkynyl, amino, aminocarbonyl, aryl, arylalkenyl, arylalkoxy, aryloxy, aryloxycarbonyl, arylsulfinyl, arylsulfonyl, arylthio, carboxy, cyano, formyl, halogen, haloalkoxy, heterocyclyl, hydroxy, mercapto, nitro, and the like, appended to any carbon atom of the alkyl moiety. In the case R^9 is arylalkylcarbonyl, the alkyl group of this radical can for example be substituted by cyclohexyl.

The term "lower alkyl", as used herein, alone or in any combination, refers to alkyl groups with 1-4 carbon atoms. Representative examples of lower alkyl include, but are not limited to, methyl, ethyl, *n*-propyl, *iso*-propyl, *n*-butyl, *iso*-butyl, *tert*-butyl and the like.

The term "alkenyl", as used herein, alone or in any combination, refers to a straight or branched hydrocarbon chain containing 2-8, preferably 2-4 carbon atoms with at least one carbon-carbon double bond. Representative examples of alkenyl include, but are not limited to, ethenyl, 2-propenyl, 2-methyl-2-propenyl, 3-butenyl, 4-pentenyl, 5-hexenyl and the like.

The term "alkylenedioxy", as used herein, alone or in any combination, refers to a $-O(CH_2)_nO-$ group, wherein n is preferably 1 or 2, and wherein the oxygen atoms are

appended to two adjacent carbon atoms of the parent molecular moiety. Representative examples of alkylenedioxy include, but are not limited to, methylenedioxy, ethylenedioxy, and the like.

The term "alkynyl", as used herein, alone or in any combination, refers to a straight or branched hydrocarbon chain containing 2-8 carbon atoms with at least one carbon-carbon triple bond. Representative examples of alkynyl include, but are not limited to, 1-propynyl, 2-propynyl, 1-butynyl, 3-butynyl, 2-pentynyl, and the like.

The term "alkoxy", as used herein, alone or in any combination, refers to an alkyl group appended to the parent molecular moiety through an oxygen bridge. Representative examples of alkoxy include, but are not limited to, methoxy, ethoxy, propoxy, 2-propoxy, butoxy, *tert*-butoxy, pentyloxy, hexyloxy, and the like.

The term "alkoxyalkyl", as used herein, alone or in any combination, refers to an alkoxy group appended to the parent molecular moiety through an alkyl group. Representative examples of alkoxyalkyl include, but are not limited to, *tert*-butoxymethyl, 2-ethoxyethyl, 2-methoxyethyl, methoxymethyl, and the like.

The term "alkoxycarbonyl", as used herein, alone or in any combination, refers to an alkoxy group appended to the parent molecular moiety through a carbonyl group. Representative examples of alkoxycarbonyl include, but are not limited to, methoxycarbonyl, ethoxycarbonyl, *tert*-butoxycarbonyl, and the like.

The term "alkoxycarbonylalkyl", as used herein, alone or in any combination, refers to an alkoxycarbonyl group appended to the parent molecular moiety through an alkyl group. Representative examples of alkoxycarbonylalkyl include, but are not limited to, methoxycarbonylpropyl, ethoxycarbonylbutyl, 2-*tert*-butoxycarbonylethyl, and the like.

The term "alkylcarbonyl" or "acyl", as used herein, alone or in any combination, refers to an alkyl group appended to the parent molecular moiety through a carbonyl group.

Representative examples of alkylcarbonyl include, but are not limited to, acetyl, 1-oxopropyl, 2,2-dimethyl-1-oxopropyl, 1-oxobutyl, 1-oxopentyl, and the like.

The term "alkylcarbonylalkyl", as used herein, alone or in any combination, refers to an alkylcarbonyl group appended to the parent molecular moiety through an alkyl group. Representative examples of alkylcarbonylalkyl include, but are not limited to, 2-oxopropyl, 3,3-dimethyl-2-oxopropyl, 3-oxobutyl, 3-oxopentyl and the like.

The term "alkylcarbonyloxy", as used herein, alone or in any combination, refers to an alkylcarbonyl group appended to the parent molecular moiety through an oxygen bridge. Representative examples of alkylcarbonyloxy include, but are not limited to, acetyloxy, ethylcarbonyloxy, *tert*-butylcarbonyloxy and the like.

The term "alkylsulfinyl", as used herein, alone or in any combination, refers to an alkyl group appended to the parent molecular moiety through a sulfinyl group. Representative examples of alkylsulfinyl include, but are not limited to, methylsulfinyl, ethylsulfinyl and the like.

The term "alkylsulfinylalkyl", as used herein, alone or in any combination, refers to an alkylsulfinyl group appended to the parent molecular moiety through an alkyl group. Representative examples of alkylsulfinylalkyl include, but are not limited to, methylsulfinylmethyl, ethylsulfinylmethyl and the like.

The term "alkylsulfonyl", as used herein, alone or in any combination, refers to an alkyl group appended to the parent molecular moiety through a sulfonyl group. Representative examples of alkylsulfonyl include, but are not limited to, methylsulfonyl, ethylsulfonyl, and the like.

The term "alkylsulfonylalkyl", as used herein, alone or in any combination, refers to an alkylsulfonyl group appended to the parent molecular moiety through an alkyl group. Representative examples of alkylsulfonylalkyl include, but are not limited to, methylsulfonylmethyl, ethylsulfonylmethyl and the like.

The term "alkylthio" (synonym "alkylsulfanyl"), as used herein, alone or in any combination, refers to an alkyl group appended to the parent molecular moiety through an -S- bridge. Representative examples of alkylthio include, but are not limited to, methylthio, ethylthio, *tert*-butylthio, hexylthio and the like.

The term "alkylthioalkyl" (synonym "alkylsulfanylalkyl"), as used herein, alone or in any combination, refers to an alkylthio group appended to the parent molecular moiety through an alkyl group. Representative examples of alkylthioalkyl include, but are not limited to, methylthiomethyl, 2-(ethylthio)ethyl, and the like.

The term "aminoalkyl", as used herein, alone or in any combination, refers to an amino group appended to the parent molecular moiety through an alkyl group. Representative examples of aminoalkyl include, but are not limited to, aminomethyl, 2-(amino)ethyl, and the like.

The term "aminocarbonyl" or "carbamoyl", as used herein, alone or in any combination, refers to an amino group appended to the parent molecular moiety through a carbonyl group.

The term "aminocarbonylalkyl", as used herein, alone or in any combination, refers to an aminocarbonyl group appended to the parent molecular moiety through an alkyl group.

The term "aryl", as used herein, alone or in any combination, refers to an carbocyclic group having at least one aromatic ring, *e.g.* phenyl or biphenyl, or multiple condensed ring systems, in which at least one ring is aromatic, *e.g.* 1,2,3,4-tetrahydronaphthyl, naphthyl, anthryl, phenanthryl, fluorenyl, and the like. The term preferably relates to phenyl or naphthyl, especially to phenyl. The aryl group may be optionally substituted with one or more functional groups individually and independently selected from alkenyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, cycloalkyl, alkylcarbonyl, alkylcarbonylalkyl, alkylcarbonyloxy, alkylendioxy, alkylsulfinyl,

--alkylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, alkylthio, alkylthioalkyl, alkynyl, amino, aminoalkyl, aminocarbonyl, aminocarbonylalkyl, aryl, arylalkenyl, arylalkoxy, arylalkyl, aryloxy, aryloxycarbonyl, aryloxycarbonylalkyl, arylsulfinyl, arylsulfinylalkyl, arylsulfonyl, arylsulfonylalkyl, arylthio, arylthioalkyl, carboxy, carboxyalkyl, cyano, cyanoalkyl, formyl, formylalkyl, halogen, haloalkoxy, haloalkyl, heterocyclyl (preferably piperidinyl), hydroxy, hydroxyalkyl, mercapto, nitro, and the like.

The term "arylalkenyl", as used herein, alone or in any combination, refers to an aryl group appended to the parent molecular moiety through an alkenyl group. The aryl group may be unsubstituted or substituted. Representative examples of arylalkenyl include, but are not limited to, 2-phenylethenyl, 3-phenylpropen-2-yl, 2-naphth-2-ylethenyl, and the like.

The term "arylalkoxy", as used herein, alone or in any combination, refers to an aryl group appended to the parent molecular moiety through an alkoxy group. The aryl group may be unsubstituted or substituted. Representative examples of arylalkoxy include, but are not limited to, 2-phenylethoxy, 5-phenylpentyloxy, 3-naphth-2-ylpropoxy, and the like.

The term "arylalkyl", as used herein, alone or in any combination, refers to an aryl group appended to the parent molecular moiety through an alkyl group. The aryl group may be unsubstituted or substituted. Representative examples of arylalkyl include, but are not limited to, benzyl, 2-phenylethyl, 3-phenylpropyl, 2-naphth-2-ylethyl, and the like.

The term "aryloxy", as used herein, alone or in any combination, refers to an aryl group appended to the parent molecular moiety through an oxygen bridge. The aryl group can be unsubstituted or substituted. Representative examples of aryloxy include, but are not limited to, phenoxy, naphthyloxy, 3-bromophenoxy, 4-chlorophenoxy, 4-methylphenoxy, 3,4-dimethoxyphenoxy, and the like.

The term "carbonyl", as used herein, alone or in any combination, refers to a -C(O)- group.

The term "carboxy", as used herein, alone or in any combination, refers to a $-CO_2H$ group.

The term "carboxyalkyl", as used herein, alone or in any combination, refers to a carboxy group appended to the parent molecular moiety through an alkyl group. Representative examples of carboxyalkyl include, but are not limited to, carboxymethyl, 2-carboxyethyl, 3-carboxypropyl, and the like.

The term "cyano", as used herein, alone or in any combination, refers to a -C≡N group.

The term "cyanoalkyl", as used herein, alone or in any combination, refers to a cyano group appended to the parent molecular moiety through an alkyl group. Representative examples of cyanoalkyl include, but are not limited to, cyanomethyl, 2-cyanoethyl, 3-cyanopropyl, and the like.

The term "cycloalkyl", as used herein, alone or in any combination, refers to a saturated cyclic hydrocarbon moiety containing 3-15, preferably 3-6, carbon atoms, optionally (less preferred) substituted with one or more groups, each individually and independently selected from alkenyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylcarbonyl, alkylcarbonylalkyl, alkylcarbonyloxy, alkylendioxy, alkylsulfinyl, alkylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, alkylthio, alkylthioalkyl, alkynyl, amino, aminoalkyl, aminocarbonyl, aminocarbonylalkyl, aryl, arylalkenyl, arylalkoxy, arylalkyl, aryloxy, aryloxycarbonyl, aryloxycarbonylalkyl, arylsulfinyl, arylsulfinylalkyl, arylsulfonyl, arylsulfonylalkyl, arylthio, arylthioalkyl, carboxy, carboxyalkyl, cyano, cyanoalkyl, formyl, formylalkyl, halogen, haloalkoxy, haloalkyl, heterocyclyl, hydroxy, hydroxyalkyl, mercapto, nitro, and the like. Representative examples of cycloalkyl include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, cyclooctyl and the like.

In polycyclic cycloalkyl groups one of the distal rings may be aromatic, *e.g.*, 1-indanyl, 2-indanyl, tetrahydronaphthyl, bicyclo[4.2.0]octa-1,3,5-trien-7-yl, and the like.

The term "formyl", as used herein, alone or in any combination, refers to a -C(O)H group.

The term "formylalkyl", as used herein, alone or in any combination, refers to a formyl group, appended to the parent molecular moiety through an alkyl group. Representative examples of formylalkyl include, but are not limited to, formylmethyl, 2-formylethyl, and the like.

The term "halo" or "halogen", as used herein, alone or in any combination, refers to fluorine, bromine, chlorine, and iodine.

The term "haloalkyl", as used herein, alone or in any combination, refers to an alkyl group having at least one hydrogen atom replaced with a halogen atom. Representative examples of haloalkyl include, but are not limited to, chloromethyl, 2-fluoroethyl, trifluoromethyl, pentafluoroethyl, 2-chloro-3-fluoropentyl, and the like.

The term "haloalkoxy", as used herein, alone or in any combination, refers to an alkoxy group having at least one hydrogen atom replaced with a halogen atom. Representative examples of haloalkoxy include, but are not limited to, chloromethoxy, 2-fluoroethoxy, trifluoromethoxy, pentafluoroethoxy, and the like.

The term "heterocyclyl", as used herein, alone or in any combination, refers to a monocyclic, bicyclic or polycyclic ring system containing up to 15 ring atoms, at least one of these, preferably 1 or 2, being a hetero atom independently selected from nitrogen, oxygen or sulfur. The ring system may be saturated, partially unsaturated, unsaturated or aromatic, mono- or bicyclic. Representative examples of heterocyclyl include, but are not limited to, furyl, imidazolyl, imidazolinyl, imidazolidinyl, isothiazolyl, isoxazolyl, morpholinyl, oxadiazolyl, oxazolyl, oxazolinyl, oxazolidinyl, piperazinyl, piperidinyl, pyranyl, pyrazinyl, pyrazolyl, pyridyl, pyrimidinyl,

pyridazinyl, pyrrolyl, pyrrolinyl, pyrrolidinyl, tetrahydrofuranyl, tetrahydrofuranyl, tetrahydrothienyl, thiadiazolyl, thiazolyl, thiazolinyl, thiazolidinyl, thienyl, thiomorpholinyl, 1,1-dioxothiomorpholinyl, benzimidazolyl, phthalazinyl, benzothiazolyl, benzothienyl, benzoxazolyl, benzofuranyl, indolyl, indolinyl, indazolyl, isobenzofuranyl, isobenzothienyl, isoindolyl, isoindolinyl, isoquinolinyl, quinolinyl, quinazolinyl and the like. Defined heterocyclyl moieties may be optionally substituted with one or more groups, each individually and independently selected from alkenyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, alkoxycarbonylalkyl, alkyl, alkylcarbonyl, alkylcarbonylalkyl, alkylcarbonyloxy, alkylendioxy, alkylsulfinyl, alkylsulfinylalkyl, alkylsulfonyl, alkylsulfonylalkyl, alkylthio, alkylthioalkyl, alkynyl, amino, aminoalkyl, aminocarbonyl, aminocarbonylalkyl, aryl, arylalkenyl, arylalkoxy, arylalkyl, aryloxy, arylcarbonyl, arylalkylcarbonyl, (diaryl)alkylcarbonyl, aryloxycarbonyl, aryloxycarbonylalkyl, arylsulfinyl, arylsulfinylalkyl, arylsulfonyl, arylsulfonylalkyl, arylthio, arylthioalkyl, carboxy, carboxyalkyl, cyano, cyanoalkyl, cycloalkyl, cycloalkylcarbonyl, cycloalkylalkylcarbonyl, formyl, formylalkyl, halogen, haloalkoxy, haloalkyl, heterocyclyl, heterocyclylcarbonyl, hydroxy, hydroxyalkyl, mercapto, nitro, and the like. Preferably the substituents are selected from oxo, alkoxycarbonyl, alkylcarbonyl, alkylsulfonyl, arylalkylcarbonyl, arylalkoxycarbonyl, arylalkylsulfonyl, arylcarbonyl, (diaryl)-alkylcarbonyl, arylsulfonyl, arylalkenylsulfonyl, cycloalkylalkylcarbonyl, cycloalkylcarbonyl, heterocyclylcarbonyl, and heterocyclylsulfonyl.

The term "saturated heterocyclyl" is another special case of "heterocyclyl" and refers to saturated rings as defined above for "heterocyclyl", especially to piperidinyl and pyrrolidinyl.

The term "heterocyclylalkenyl", as used herein, alone or in any combination, refers to a heterocyclyl group appended to the parent molecular moiety through an alkenyl group. Representative examples of heterocyclylalkenyl include, but are not limited to, 2-pyrid-3-ylethenyl, 3-quinolin-3-ylpropen-2-yl, 5-pyrid-4-ylpenten-4-yl, and the like.

The term "heterocyclylalkoxy", as used herein, alone or in any combination, refers to a heterocyclyl group appended to the parent molecular moiety through an alkoxy group. Representative examples of heterocyclylalkoxy include, but are not limited to, 2-pyrid-3-ylethoxy, 3-quinolin-3-ylpropoxy, 5-pyrid-4-ylpentyloxy, and the like.

The term "heterocyclylalkyl", as used herein, alone or in any combination, refers to a heterocyclyl group appended to the parent molecular moiety through an alkyl group. Representative examples of heterocyclylalkyl include, but are not limited to, 2-pyrid-3-ylmethyl, 2-pyrimidin-2-ylpropyl, and the like.

The term "heterocyclyloxy", as used herein, alone or in any combination, refers to a heterocyclyl group appended to the parent molecular moiety through an oxy group. Representative examples of heterocyclyloxy include, but are not limited to, pyrid-3-yloxy, quinolin-3-yloxy, and the like, especially (1-ethyloxycarbonyl-indazol-3-yl)-oxy.

The term "hydroxy" or "hydroxyl" as used herein, alone or in any combination, refers to an -OH group

The term "hydroxyalkyl", as used herein, alone or in any combination, refers to an alkyl group having at least one hydrogen atom replaced with a hydroxy group. Representative examples of hydroxyalkyl include, but are not limited to, hydroxymethyl, 2-hydroxyethyl, 3-hydroxypropyl, 2-ethyl-4-hydroxyheptyl, and the like.

The term "nitro", as used herein, alone or in any combination, refers to a $-NO_2$ group.

The term "oxo", as used herein, alone or in any combination, refers to an =O group.

The term "oxy", as used herein, alone or in any combination, refers to an -O- group.

The terms "mercapto" and "thiol", as used herein, alone or in any combination, refer to a -SH group.

The terms "thio" (synonym "sulfanyl"), "sulfinyl" and "sulfonyl", as used herein, alone or in any combination, refer to a $-S(O)_n$ group with n= 0, 1 and 2, respectively.

Within the scope of the present invention, unless indicated otherwise, compounds of Formula I or pharmaceutically acceptable salts thereof are included that may exist in, and be isolated in, isomeric forms, including *cis*- or *trans* isomers or mixtures thereof, and tautomers. Other compounds of this invention may contain one or more stereogenic or asymmetric centers, such as one or more asymmetric carbon atoms, and thus may give rise to optically pure enantiomers, mixtures of enantiomers, racemates, enantiomer-pure diastereomers, mixtures of diastereomers, epimers, and other stereoisomeric forms that may be defined, in terms of absolute stereochemistry, as (*R*)-, (*S*)- or (*R*,*S*)-configured, preferably in the (*R*)- or (*S*)-configuration. Such isomers can be obtained by methods within the knowledge of one skilled in the art, *e.g.* by stereochemically controlled synthesis using chiral synthons or chiral reagents, or by means of classical separation techniques, such as chromatographic or crystallization methods, or by other methods known in the art, such as through formation of diastereomeric salts, for example by salt formation with an enantiomerically pure chiral acid, or by means of chromatography, for example by using chromatographic materials modified with chiral ligands. Furthermore, the present invention refers to compounds containing centers of any geometric asymmetry, like, for example, unsymmetrically substituted olefinic double bond, including E or Z geometric isomers and mixtures thereof. Generally, pure isomers of compounds of Formula I are preferred over isomeric mixtures.

In the present invention, the compounds of Formula I may be used in the form of pharmaceutically acceptable salts. The term "pharmaceutically acceptable salts" refers to relatively nontoxic, inorganic or organic acid and base addition salts, which retain the biological effectiveness and properties of the parent compound, and which are not

biologically or otherwise undesirable (see, *e.g.*, Berge et al., J. Pharm. Sci. 1977, 66, 1-19).

Certain compounds of the present invention can contain one or more basic functional groups, such as amino, alkylamino, or arylamino, and, thus, be capable of forming pharmaceutically acceptable acid addition salts. These acid addition salts may be prepared by standard procedures in a suitable solvent from the parent compound of Formula I, with an appropriate amount of an inorganic acid, including, but not limited to, for example, hydrochloric acid, hydrobromic acid, sulfuric acid, or phosphoric acid; or of an organic acid, including, but not limited to, acetic acid, propionic acid, octanoic acid, decanoic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, ascorbic acid, amino acids, such as glutamic acid or aspartic acid, benzoic acid, cinnamic acid, salicylic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, *p*-toluenesulfonic acid, or other acidic organic compounds.

Certain compounds of the present invention may, on the other hand, contain one or more acidic functional groups and, thus, be capable of forming pharmaceutically acceptable base addition salts. These salts can be prepared by addition of an appropriate amount, usually in stoichiometric ratio, of an alkaline reagent, such as hydroxide, carbonate or alkoxide, containing the appropriate cation, to the free acid in a suitable solvent. Preferred inorganic salts include, but are not limited to, ammonium, sodium, potassium, calcium or magnesium, also zinc salts and the like. Preferred salts derived from organic bases include, but are not limited to, salts of primary, secondary, and tertiary amines, substituted amines, cyclic amines, and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, ethanolamine, lysine, arginine, *N*-ethylpiperidine, piperidine, polyamine resins, and the like.

Compounds of the present invention containing both acidic and basic groups can also form internal salts (zwitter ions).

For isolation or purification purposes, it is also possible to use pharmaceutically unacceptable salts, for example perchlorates, picolinates, picrates, or the like. For therapeutic use, only pharmaceutically acceptable salts or free compounds are employed, where applicable in the form of pharmaceutical preparations, and these are therefore preferred.

Certain compounds of Formula I, including their salts, may exist in solvated as well as unsolvated forms, such as, for example, hydrated forms, or their crystals may, for example, include the solvent used for crystallization. Different crystalline forms may be present. The present invention encompasses all such solvated and unsolvated forms.

The present invention also relates to prodrug derivatives of the parent compounds of Formula I. The term "prodrug" refers to pharmacologically inactive precursors of a drug that may be converted into its therapeutically active form under physiological conditions *in vivo*, for example, when they undergo solvolysis, or enzymatic degradation in blood, or in cells (Bundgard H., "Design of Prodrugs", pp. 7-9, 21-24, Elsevier, Amsterdam (1985); Silverman R. B., "The Organic Chemistry of Drug Design and Drug Action", pp. 352-401, Academic Press, San Diego, CA (1992); Higuchi T. et al., "Pro-drug as Novel Delivery Systems", A.C.S. Symposium Series, Vol. 14). The term "prodrug" also includes any covalently bonded carriers, which release the active parent compound *in vivo* when administered to a mammal. Prodrug modifications of a compound often offer advantages of solubility, bioavailability, absorption, tissue compatibility, tissue distribution, or delayed release in the mammalian organism. Prodrugs are variations or derivatives of the compounds of Formula I, which have groups cleavable under metabolic conditions, for example, pharmaceutically acceptable esters, or amides. Such groups can be cleaved enzymatically or non-enzymatically, or hydrolytically to the free hydroxy, carboxy, or amino group of the active parent compound. In another embodiment, the prodrug is a reduced form, which is oxidized *in vivo* to the therapeutic compound, for example, a thiol, which is oxidized to a sulfonate or sulfate, or an alcohol, which is oxidized to a carboxylic acid.

Further included within the scope of the present invention are pharmaceutically acceptable esters of the compounds of Formula I. The term "pharmaceutically acceptable esters" refers to relatively non-toxic, esterified products of the parent compound. These esters can be prepared *in situ* during the final isolation and purification of the compounds, or by separately reacting the purified compounds in its free acid or hydroxyl form with a suitable esterifying agent. Carboxylic acids can be converted into esters *via* treatment with an alcohol in the presence of a catalyst. Hydroxyl containing derivatives can be converted into esters *via* treatment with an esterifying agent such as alkanoyl halides. The term further includes lower hydrocarbon groups capable of being solvated under physiological conditions, for example, alkyl esters, preferred methyl, ethyl, and propyl esters, methoxymethyl esters, methylthiomethyl esters, pivaloyloxymethyl esters and the like (see, *e.g.*, Berge et al., J. Pharm. Sci. 1977, 66, 1-19).

The compounds of the present invention have useful, in particular pharmacologically useful, properties. They are able to specifically antagonize the effect of endogenous PGD_2 on the CRTH2 receptor, and may be used for the prevention and/or treatment of chronic and acute allergic immune disorders comprising allergic asthma, rhinitis, chronic obstructive pulmonary disease (COPD), dermatitis, inflammatory bowel disease, rheumatoid arthritis, allergic nephritis, conjunctivitis, atopic dermatitis, bronchial asthma, food allergy, systemic mast cell disorders, anaphylactic shock, urticaria, eczema, itching, inflammation, ischemia-reperfusion injury, cerebrovascular disorders, pleuritis, ulcerative colitis, eosinophil-related diseases comprising Churg-Strauss syndrome and sinusitis, basophil-related diseases, comprising basophilic leukemia and basophilic leukocytosis in humans and other mammals.

A compound or a pharmaceutical composition of the invention may thus be used as a drug (medicine) or therapeutic agent for prevention and/or treatment of both chronic and acute allergic/immune disorders such as those mentioned above, especially allergic asthma, rhinitis, COPD, dermatitis, inflammatory bowel disease, and rheumatoid arthritis.

In another aspect, the compounds of Formula I may be used as standard or reference compounds in tests or assays involving the inhibition of the CRTH2 receptor. Such compounds could be made commercially available for use as a reference, quality standard or control, for example in pharmaceutical research when developing new assays or protocols related to CRTH2 activity.

As mentioned earlier, compounds of Formula I, or salts, or prodrugs thereof, antagonize the PGD_2 activation of the CRTH2 receptor. The biological effect of such compounds may be tested in a variety of *in vitro*, *ex vivo* and *in vivo* assays.

The ability of the compounds of Formula I to bind to the CRTH2 receptor may be measured by methods similar to those described in Sawyer N. et al., *Br. J. Pharmacol.*, 2002, 137, 1163-1172 and by the method described below in the experimental part.

With this type of assay, IC_{50} values (*i.e.* the concentrations where half-maximal inhibition of the interaction is found) in the range of 0.001 to 10 μM, preferably values below 1 μM, in particular values below 0.05 μM, are found with test compounds of Formula I. Exemplary IC_{50} values determined in this test are given below in Table 68.

A functional assay with cells expressing the human CRTH2 receptor may be used to detect changes in the levels of intracellular calcium concentration following compound treatment. After addition of the compound the cells are challenged with PGD_2. In a Fluorescent Imaging Plate Reader (FLIPR™, Molecular Devices, Sunnyvale, California) fluorescence emission is recorded during both additions, emission peak values above base level after PGD_2 addition were exported, normalized to low controls (no PGD_2) and high controls (no active compound). The relative values of the remaining activity were used to determine IC_{50} values by curve fitting the data to a single site to a four-parameter logistic sigmoid dose response curve of the equation (A+((B-A)/(1+((C/x)^D)))).

The ability of the compounds to inhibit PGD_2 induced change of intracellular calcium levels *via* CRTH2 activation may be measured by methods known of one skilled in the art or by the method described below in the experimental part.

With this assay, IC_{50} values (*i.e.* the concentration of a compound at which the remaining activity is 50%) in the range of 0.001 and 10 μM, preferably below 0.5 μM, are obtained with test compounds of Formula I. Exemplary IC_{50} values determined in this test are given below in Table 69.

The results of these assays clearly demonstrate, that the present invention provides functional antagonists of the PGD_2 receptor.

On the basis of the biological studies discussed hereinabove, a compound of Formula I according to the invention may show therapeutic efficacy against chronic and acute allergic/immune disorders such as allergic asthma, rhinitis, chronic obstructive pulmonary disease (COPD), dermatitis, inflammatory bowel disease, and rheumatoid arthritis.

A compound of Formula I, a pharmaceutically acceptable salt or a prodrug thereof, can be administered alone in pure form or in combination with one or more other therapeutic agents, possible combination therapy taking the form of fixed combinations or the administration of a compound of the invention and one or more other therapeutic agents being staggered or given independently of one another, or the combined administration of fixed combinations and one or more other therapeutic agents. A compound of Formula I can besides or in addition be administered especially for prevention and/or treatment of both chronic and acute allergic or immune disorders in combination with other inflammatory diseases. Long-term therapy is equally possible as is adjuvant therapy in the context of other treatment strategies, as described above. Other possible treatments are preventive therapies, for example in patients at risk.

The invention relates also to pharmaceutical compositions comprising compounds of Formula I, to their use in therapeutic, in a broader aspect of the invention also prophylactic treatment or a method of treatment of the diseases mentioned above, to the compounds for said use and to the preparation of pharmaceutical formulations (medicines).

The pharmaceutically acceptable compounds of the present invention may be used, for example, for the preparation of pharmaceutical compositions that comprise an effective amount of the active ingredient together or in admixture with a significant amount of one or more inorganic, organic, solid or liquid, pharmaceutically acceptable carriers.

The invention relates also to a pharmaceutical composition that is suitable for administration to a warm-blooded animal, especially a human (or to cells or cell lines derived from a warm-blooded animal, especially a human, for the treatment or, in a broader aspect of the invention, prevention of (*i.e.* prophylaxis against) a disease that responds to blockade of the interaction of the CRTH2 receptor with PGD_2, comprising an amount of a compound of Formula I or a pharmaceutically acceptable salt or a prodrug thereof, which is effective for said inhibition, together with at least one pharmaceutically acceptable carrier.

The pharmaceutical compositions according to the invention are those for enteral administration, such as nasal, buccal, rectal, dermal or, especially oral administration, and for parenteral administration, such as intramuscular, intravenous or subcutaneous, intrasternal, intravitreal, injection or infusion, to warm-blooded animals, especially humans. Such compositions comprise an effective dose of the pharmaceutically active ingredient, alone or together with a significant amount of a pharmaceutically acceptable carrier. The dosage of the active ingredient depends on the species of warm-blooded animal, the body weight, the age and the individual conditions, individual pharmacokinetic data, the disease to be treated and the mode of administration.

The invention relates also to a process or a method for the treatment of a pathological condition mentioned hereinabove, especially a disease, which responds to blockade of the interaction of the CRTH2 receptor with PGD_2, especially allergic asthma, rhinitis, chronic obstructive pulmonary disease (COPD), dermatitis, inflammatory bowel disease, and rheumatoid arthritis. The compounds of Formula I or salts or prodrugs thereof can be administered as such or especially in the form of pharmaceutical compositions.

The dose to be administered to warm-blooded animals, for example humans of approximatively 70 kg body weight, is preferably from approximatively 3 mg to approximatively 30 g, more preferably from approximatively 10 mg to approximatively 1000 mg per person per day, divided preferably into 1 to 3 single doses which may, for example, be of the same size. The amount of the compound actually administered will typically be determined by a physician, in the light of the relevant circumstances, including the condition to be treated, the chosen route of administration, the actual compound administered, the age, the weight, and response of the individual patient, the severity of the patient's symptoms, and the like, for example, children usually receive half of the adults dose.

The pharmaceutical compositions comprise from approximately 1% to approximately 95%, preferably from approximately 20% to approximately 90%, active ingredient. Pharmaceutical compositions according to the invention may be, for example, in unit dosage forms such as coated and uncoated tablets, pills, ampoules, vials, suppositories, dragées, or capsules. Further dosage forms are, for example, ointments, creams, pastes, emulsions, foams, chewable gums, tinctures, lip-sticks, drops, sprays or aerosols, syrups or elixirs, dispersions, transdermal patches or pads, or *via* an intravitreal device that releases the compound in a sustained capacity, and the like. Examples are capsules containing from about 0.05 g to about 1.0 g active ingredient.

The pharmaceutical compositions of the present invention are prepared in a manner known, *per se*, for example by means of conventional mixing, granulating, coating, dissolving, lyophilizing or confectioning processes.

Solutions of the active ingredient, and also suspensions, and especially isotonic aqueous solutions or suspensions, are preferably used, it being possible, for example in the case of lyophilized compositions, that comprise the active ingredient alone or together with a carrier, for example mannitol, for such solutions or suspensions to be produced prior to use. The pharmaceutical compositions may be sterilized and/or may comprise excipients, for example preservatives, stabilizers, wetting agents and/or

emulsifiers, solubilizers, salts for regulating osmotic pressure and/or buffers and are prepared in a manner known *per se*, for example by means of conventional dissolving or lyophilizing processes. The said solutions or suspensions may comprise viscosity-increasing substances, such as sodium carboxymethylcellulose, carboxymethylcellulose, dextran, polyvinylpyrrolidone or gelatin.

Suspensions in oil comprise as the oil component the vegetable, synthetic or semi-synthetic oils customary for injection purposes. There may be mentioned as such especially liquid fatty acid esters that contain as the acid component a long-chain fatty acid having from 8 to 22, especially from 12 to 22, carbon atoms, for example lauric acid, tridecylic acid, myristic acid, pentadecylic acid, palmitic acid, margaric acid, stearic acid, arachidic acid, behenic acid or corresponding unsaturated acids, for example oleic acid, elaidic acid, erucic acid, brasidic acid or linoleic acid, if desired with the addition of antioxidants, for example vitamin E, β-carotene or 3,5-di-*tert*-butyl-4-hydroxytoluene. The alcohol component of those fatty acid esters has a maximum of 6 carbon atoms and is mono- or poly-hydroxy, for example a mono-, di- or trihydroxy, alcohol, for example methanol, ethanol, propanol, butanol, or pentanol or the isomers thereof, but especially glycol and glycerol. The following examples of fatty acid esters are therefore to be mentioned: ethyl oleate, isopropyl myristate, isopropyl palmitate, "Labrafil M2375" (polyoxyethylene glycerol trioleate, Gattefossé, Paris), "Miglyol 812" (triglyceride of saturated fatty acids with chain length of C8 to C12, Hüls AG, Germany), but especially vegetable oils, such as cottonseed oil, almond oil, olive oil, castor oil, sesame oil, soybean oil and more especially groundnut oil.

The injection or infusion compositions are prepared in customary manner under sterile conditions; the same applies also to introducing the compositions into ampoules or vials and sealing the containers.

Pharmaceutical compositions for oral administration can be obtained by combining the active ingredient with solid carriers, if desired granulating a resulting mixture, and processing the mixture, if desired or necessary, after the addition of appropriate excipients, into tablets, dragée cores or capsules. It is also possible for them to be

incorporated into plastics carriers that allow the active ingredients to diffuse or be released in measured amounts.

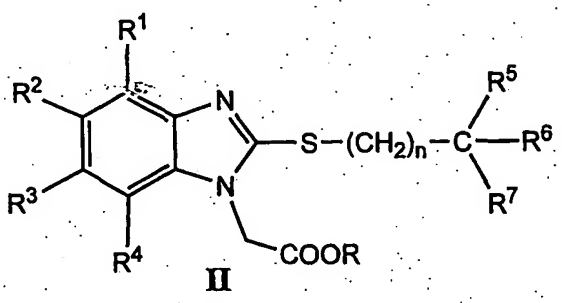
Suitable carriers are especially fillers, such as sugars, for example lactose, saccharose, mannitol or sorbitol, cellulose preparations and/or calcium phosphates, for example tricalcium phosphate or calcium hydrogen phosphate, and binders, such as starch pastes using for example corn, wheat, rice, or potato starch, gelatin, tragacanth, methylcellulose, hydroxypropylmethylcellulose, sodium carboxymethylcellulose and/or polyvinylpyrrolidone, and/or, if desired, disintegrators, such as the above-mentioned starches, and/or carboxymethyl starch, crosslinked polyvinylpyrrolidone, agar, alginic acid or a salt thereof, such as sodium alginate. Excipients are especially flow conditioners and lubricants, for example silicic acid, talc, stearic acid or salts thereof, such as magnesium or calcium stearate, and/or polyethylene glycol. Dragée cores are provided with suitable, optionally enteric, coatings, there being used, inter alia, concentrated sugar solutions which may comprise gum Arabic, talc, polyvinylpyrrolidone, polyethylene glycol, and/or titanium dioxide, or coating solutions in suitable organic solvents, or, for the preparation of enteric coatings, solutions of suitable cellulose preparations, such as ethylcellulose phthalate or hydroxypropylmethylcellulose phthalate. Capsules are dry-filled capsules made of gelatin and of soft sealed capsules made of gelatine and a plasticiser, such as glycerol or sorbitol. The dry-filled capsules may comprise the active ingredient in the form of granules, for example with fillers, such as lactose, binders, such as starches, and/or glidants, such as talc or magnesium stearate, and if desired with stabilizers. In soft capsules the active ingredient is preferably dissolved or suspended in suitable oil excipients, such as fatty oils, paraffin oil or liquid polyethylene glycols, it being possible also for stabilizers and/or antibacterial agents to be added. Dyes or pigments may be added to the tablets or dragée coatings or the capsule casings, for example for identification purposes or to indicate different doses of active ingredient.

For parenteral administration, aqueous solutions of an active ingredient in water-soluble form, for example of a water-soluble salt, or aqueous injection suspensions that contain viscosity-increasing substances and stabilizers, are especially suitable. The

active ingredient, optionally together with excipients, can also be in the form of a lyophilizate and be made into a solution before parenteral administration by the addition of solvents.

The novel compounds of Formula I can be manufactured in accordance with the invention by

a) hydrolyzing a precursor of the general Formula II



II

wherein R^1-R^7 and n are as in Formula I and R represents an alkyl group, preferably ethyl or *tert*-butyl, with the exception of:

methyl [2-(5-trifluoromethyl-pyridin-2-ylsulfanyl)-benzoimidazol-1-yl]-acetate;

methyl [2-(4-chloro-benzylsulfanyl)-benzoimidazol-1-yl]-acetate;

methyl (2-benzylsulfanyl-benzoimidazol-1-yl)-acetate;

methyl [2-(5-nitro-pyridin-2-ylsulfanyl)-benzoimidazol-1-yl]-acetate;

methyl (2-methylsulfanyl-benzoimidazol-1-yl)-acetate;

ethyl (2-methylsulfanyl-benzoimidazol-1-yl)-acetate;

methyl (2-ethylsulfanyl-benzoimidazol-1-yl)-acetate;

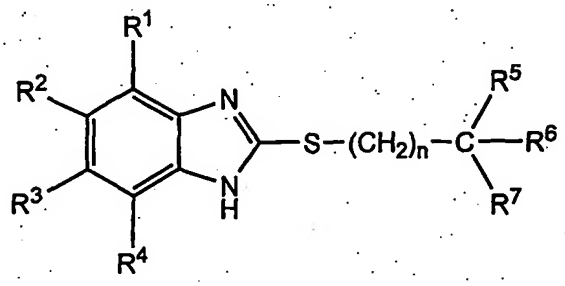
ethyl [2-(1,3,7-trimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-purin-8-ylsulfanyl)-benzoimidazol-1-yl]-acetate;

ethyl {2-[3-methyl-4-(2-morpholin-4-yl-ethylsulfanyl)-pyridin-2-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate; and

methyl {2-[3-methyl-4-(2-morpholin-4-yl-ethylsulfanyl)-pyridin-2-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate;

or

b) alkylating a benzoimidazole derivative of the general Formula



wherein R^1-R^7 and n are as in Formula I,

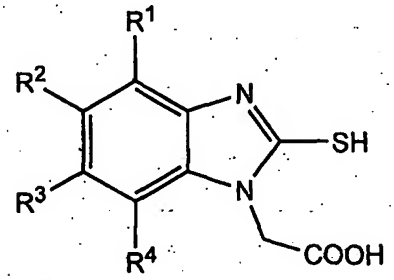
with a compound of the general Formula

$$L^1\text{-}CH_2COOH$$

wherein L^1 is a leaving group,

or

c) S-alkylating a mercapto derivative of the general Formula



wherein R^1-R^4 are as in Formula I,

with an alkylating agent of the general Formula

$$L^2\text{-}(CH_2)_n\text{-}C\text{-}R^5R^6R^7$$

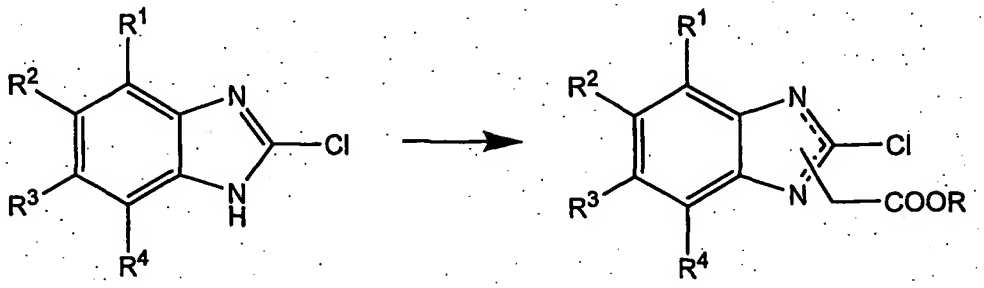
wherein R^5-R^7 and n are as in Formula I and L^2 is a leaving group,

and, if desired, converting a compound of Formula I into a pharmaceutically acceptable salt.

Compounds of the invention may be manufactured by the application or adaptation of known methods, by which is meant methods used heretofore or described in the literature, for example those described by Larock R. C. in "Comprehensive organic transformations: a guide to functional group preparations", VCH publishers, 1999.

In the reactions described hereinafter, it may be necessary to protect reactive functional groups, for example hydroxy, amino, imino, thio or carboxy groups, where these are desired in the final product, to avoid their unwanted participation in the reactions. Conventional protecting groups may be used in accordance with standard practice, for example see Greene T. W. and Wuts P. G. M. in "Protective groups in organic synthesis" Wiley-Interscience, 1999.

Generally, a synthesis of 2-sulfanyl-benzoimidazol-1-yl-acetic acid of Formula I starts by alkylating a 2-chlorobenzoimidazole of Formula **1** with a compound of Formula L^1-CH_2CO_2R, wherein R represents an alkyl group, preferably ethyl or *tert*-butyl, and L^1 is a leaving group, in a suitable polar solvent such as *N,N*-dimethylformamide, acetone, acetonitrile or the like, in the presence of a base, such as potassium carbonate, cesium carbonate, sodium hydride or the like, to yield an alkyl (2-chloro-benzoimidazol-1-yl)-acetate of Formula **2**, as outlined in Scheme 1.



1 **2**

Scheme 1

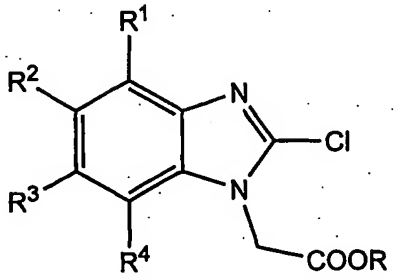
The dotted lines in Formula **2** indicate that the double bond is in either of the two possible positions; the $-CH_2COOR$ residue is connected to either of the two nitrogen

atoms; this is of significance for producing regioisomers, *i.e.* when R^1 and R^4, or R^2 and R^3, are substituents different from each other (cf. below Formulas **2a** and **2b**).

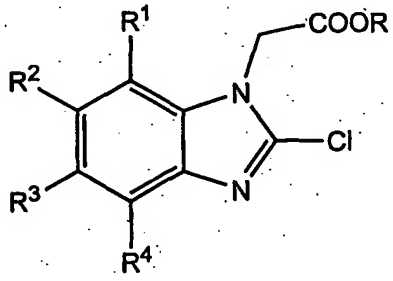
Suitable is a leaving group L^1 such as halo, in particular bromo or chloro. Preferably, a compound of Formula L^1-CH_2CO_2R is *tert*-butyl or ethyl bromoacetate.

Under preferred conditions a solution of a chlorobenzoimidazole of Formula **1** in acetone is stirred with *e.g.* *tert*-butyl bromoacetate in presence of potassium carbonate at reflux, or in DMF at room temperature.

It is noteworthy, that under such alkylating conditions an unsymmetrically substituted 2-chlorobenzoimidazole of Formula **1**, wherein R^1 and R^4, or R^2 and R^3 are different from each other, delivers a mixture of the respective C(4) and C(7), or C(5) and C(6) substituted alkyl (2-chloro-benzoimidazol-1-yl)-acetate regioisomers of Formula **2a** and **2b**.

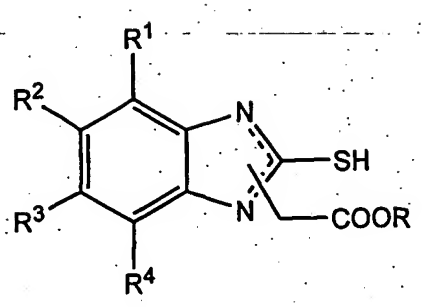


2a

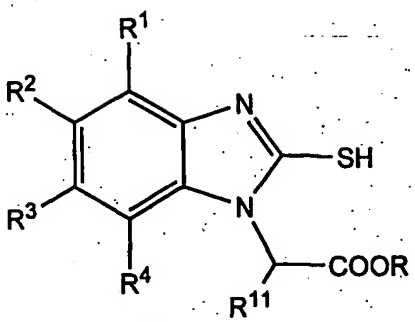


2b

Applying a procedure described by Migawa, M. T. et al., J. Med. Chem. 1998, 41, 1242-1251, an alkyl (2-chloro-benzoimidazol-1-yl)-acetate of Formula **2** is treated with thiourea in a solvent such as methanol or ethanol at reflux, to give an Intermediate of Formula **3**.



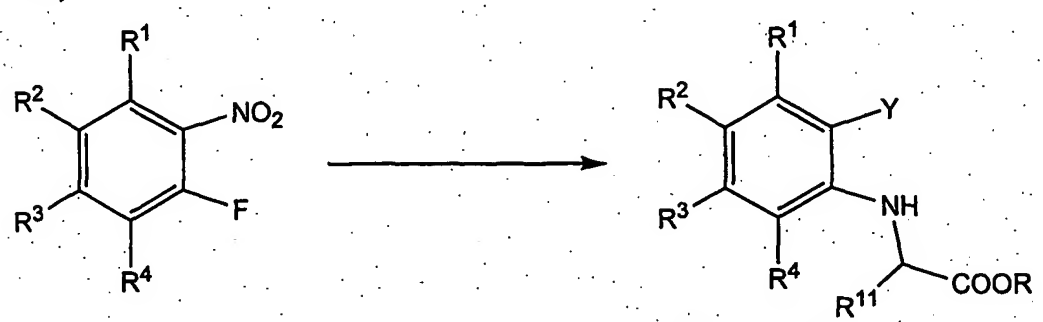
3



3a

A novel method to regioselectively produce an intermediate of Formula **3a** has been developed:

Substituted 1-fluoro-2-nitro-benzene of Formula **12** is converted to a compound of Formula **13.1** by reacting with an amino acid ester in a suitable solvent such as DMSO, EtOH or the like at elevated temperature from 50°C to 100°C (McFarlane *et al*, J. Chem. Soc. Perkin Trans. I 1988, 691-696). Subsequent hydrogenolysis with hydrogen in the presence of a catalyst such as palladium on charcoal in a solvent like tetrahydrofuran leads to a substituted aniline derivative of Formula **13.2**, which then is reacted with thiocarbonyle diimidazole to yield Intermediate **3a** (Wright, J. L. *et al*, J. Med. Chem., 2000, 43, 3408-3419; Breslin, H. J. *et al*, J. Med. Chem. 1995, 38, 771-793).



12

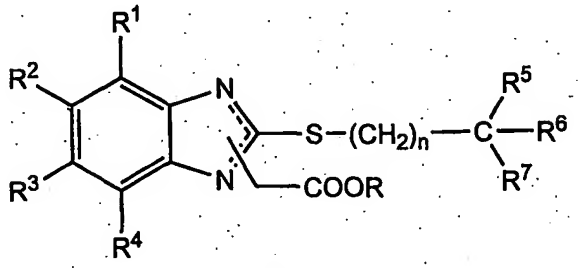
13.1 Y = NO_2
13.2 Y = NH_2

Generally, when a reaction or synthesis involves an Intermediate of Formula **3** and when obtaining the product as only one single regioisomer is wished, then an Intemediate of Formula **3a** can be used in place of an Intermediate of Formula **3**.

Subsequent S-alkylation of an Intermediate of Formula **3** occurs with a suitable alkylating agent of Formula L^2-$(CH_2)_n$-C-$R^5R^6R^7$;

wherein R^5, R^6, and R^7 and n are defined as hereinabove, and

L^2 is a leaving group such as halo, in particular chloro, bromo, or iodo; alkylsulfonate, or arylsulfonate, such as methylsulfonate, or p-toluenesulfonate;
in a solvent such as *N,N*-dimethylformamide, acetone, acetonitrile or the like,
in the presence of a base such as triethylamine, *N,N*-diisopropylethylamine, sodium hydroxide, potassium carbonate;
affording a Precursor of Formula **4**.



4

Typically, a reagent of Formula L^2-$(CH_2)_n$-C-$R^5R^6R^7$ is an optionally substituted alkyl halide, particularly an alkyl chloride, or an alkyl bromide, such as commercially available 2-(2-bromo-ethyl)-isoindole-1,3-dione; (2-bromo-ethyl)-carbamic acid *tert*-butyl ester; (3-bromo-propyl)-carbamic acid *tert*-butyl ester; (2-bromo-ethyl)-cyclohexane; 1-bromo-hexane; 1-bromo-pentane; 4-bromo-but-1-ene; 1-bromo-butane; bromo-cyclopentane; (1-bromo-ethyl)-benzene; bromo-phenyl-acetic acid methyl ester; 7-bromo-bicyclo[4.2.0]octa-1(6),2,4-triene; 2-bromo-1-phenyl-propan-1-one; 6-bromo-hexanoic acid ethyl ester; 4-bromo-butyric acid ethyl ester; 5-bromo-pentanoic acid ethyl ester; bromomethyl-benzene; 1-chloromethyl-2-methoxy-benzene; (2-bromo-ethyl)-benzene; (3-bromo-propyl)-benzene; 3,3-diphenyl-propyl bromide; 1-(2-bromo-ethoxy)-4-chloro-benzene; (2-bromo-ethoxy)-benzene; (4-bromo-butoxy)-benzene; (5-bromo-pentyloxy)-benzene; 2-(3-bromo-propyl)-isoindole-1,3-dione; 3-bromomethyl-benzoic acid methyl ester; 5-chloromethyl-furan-2-carboxylic acid ethyl ester; 1-(3-chloromethyl-4-ethoxy-phenyl)-ethanone; or 1-(3-chloromethyl-4-methoxy-phenyl)-ethanone.

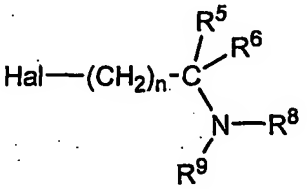
More preferred is a reagent of Formula L^2-$(CH_2)_n$-C-$R^5R^6R^7$, such as benzyl-(3-chloro-propyl)-carbamic acid *tert*-butyl ester; 5-bromo-pentanoic acid butyl-phenyl-amide; 5-bromo-1-(3,4-dihydro-2*H*-quinolin-1-yl)-pentan-1-one; 5-bromo-pentanoic acid

methyl-phenyl-amide; 1-(2-bromo-ethoxy)-naphthalene; 2-(2-bromo-ethoxy)-naphthalene; 2-(3-chloro-propyl)-2,3-dihydro-isoindol-1-one; 1-(3-chloro-propyl)-1,3-dihydro-benzoimidazol-2-one; 3-(3-chloro-propyl)-1*H*-quinazoline-2,4-dione; 2-(3-chloro-propyl)-1,1-dioxo-1,2-dihydro-1λ^6-benzo[d]isothiazol-3-one; 2-bromo-5-bromomethyl-benzoic acid methyl ester; 4-bromo-3-bromomethyl-benzoic acid methyl ester; 3-bromomethyl-4-methoxy-benzoic acid methyl ester; 1-(3-chloromethyl-4-propoxy-phenyl)-ethanone; 1-(3-chloromethyl-4-butoxy-phenyl)-ethanone; (3-chloromethyl-4-methoxy-phenyl)-phenyl-methanone; 2-chloromethyl-oxazole-4-carboxylic acid methyl ester; or 1-(3-bromomethyl-phenyl)-ethanone.

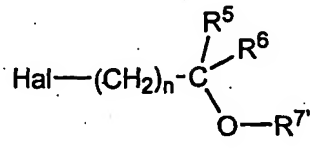
Particularly preferred is a novel alkyl halide of Formula L^2-$(CH_2)_n$-C-$R^5R^6R^7$, such as (3-chloro-propyl)-phenethyl-carbamic acid *tert*-butyl ester; (3-chloro-propyl)-(4-piperidin-1-yl-phenyl)-carbamic acid *tert*-butyl ester; 4-[*tert*-butoxycarbonyl-(3-chloro-propyl)-amino]-benzoic acid ethyl ester; (3-chloro-propyl)-cyclopropyl-carbamic acid *tert*-butyl ester; (3-chloro-propyl)-phenyl-carbamic acid *tert*-butyl ester; (3-chloro-propyl)-(2,2-diphenyl-ethyl)-carbamic acid *tert*-butyl ester; (3-chloro-propyl)-phenethyl-carbamic acid butyl ester; benzyl-(3-chloro-propyl)-carbamic acid butyl ester; (3-chloro-propyl)-cyclohexyl-carbamic acid butyl ester; (3-chloro-propyl)-cyclohexylmethyl-carbamic acid butyl ester; 4-[(3-chloro-propyl)-(2-cyclohexyl-2-phenyl-acetyl)-amino]-benzoic acid ethyl ester; pentanoic acid (3-chloro-propyl)-phenethyl-amide; 4-[butoxycarbonyl-(3-chloro-propyl)-amino]-benzoic acid ethyl ester; 5-bromo-pentanoic acid benzyl-phenyl-amide; 5-bromo-pentanoic acid benzyl-methyl-amide; 3-(3-chloro-propoxy)-indazole-1-carboxylic acid ethyl ester; 2-(3-chloro-propyl)-3-oxo-2,3-dihydro-indazole-1-carboxylic acid ethyl ester; 2-(3-chloro-propyl)-2*H*-phthalazin-1-one; 5-bromomethyl-nicotinic acid methyl ester; 2-bromomethyl-6-chloro-isonicotinic acid methyl ester; 2-bromo-3-bromomethyl-benzoic acid methyl ester; 3-bromo-5-bromomethyl-benzoic acid methyl ester; 3-methoxy-5-chloromethyl-benzoic acid isopropyl ester; 1-[3-chloromethyl-4-(3-hydroxy-propoxy)-phenyl]-ethanone; 7-chloromethyl-6-methoxy-3,4-dihydro-2H-naphthalen-1-one; and 1-(3-chloromethyl-piperidin-1-yl)-butan-1-one.

Preferred alkyl halides of Formula L^2-$(CH_2)_n$-C-$R^5R^6R^7$ are depicted in Formula **5.1** and **5.2**. Such compounds can either be prepared and isolated as such, or generated *in situ*, from a dihaloalkane of Formula Hal^1-$(CH_2)_n$-Hal^2, wherein Hal^1 and Hal^2 represent halo, independently selected from chloro, bromo, or iodo; such as 1-chloro-2-iodo-ethane, 1,2-dibromo-ethane, or 1,2-dichloro-ethane; 1-chloro-3-iodo-propane, 1,3-dibromo-propane, or 1,3-dichloropropane; 1-chloro-4-iodo-butane, 1,4-dibromo-butane, or 1,4-dichloro-butane; with a substituted amine of hereinabove defined Formula HNR^8R^9, whereby R^8 and R^9 both are not hydrogen, such as alkylcarbonyl-aryl-amine, alkoxycarbonyl-arylalkyl-amine, alkoxycarbonyl-arylamine, alkoxycarbonyl-cyclylalkyl-amine, alkoxycarbonyl-cycloalkyl-amine, arylalkylcarbonyl-aryl-amine, alkylsulfonyl-alkylamine, arylalkylsulfonyl-alkylamine, arylsulfonyl-alkylamine, alkylsulfonyl-cycloalkylamine, arylalkylsulfonyl-cycloalkylamine, arylsulfonyl-cycloalkylamine, alkylsulfonyl-arylalkylamine, arylalkylsulfonyl-arylalkylamine, arylsulfonyl-arylalkylamine, alkylsulfonyl-arylamine, arylalkylsulfonyl-arylamine, arylsulfonyl-arylamine, 1,3-dihydro-benzoimidazol-2-one, 2,3-dihydro-isoindol-1-one, 1,1-dioxo-1,2-dihydro-1λ^6-benzo[d]isothiazol-3-one, isoindole-1,3-dione, 3-oxo-2,3-dihydro-indazole-1-carboxylic acid ethyl ester, 1*H*-quinazoline-2,4-dione, 2*H*-phthalazin-1-one; or with a hydroxy-arene of Formula $HOR^{7'}$, wherein $R^{7'}$ represents a substituted phenyl, naphthyl or heterocyclyl such as indazol-3-yl-1-carboxylic acid ethyl ester; in a polar solvent such as *N,N*-dimethylformamide, tetrahydrofuran or acetonitrile; in the presence of a base such as sodium hydride, potassium *tert*-butylate.

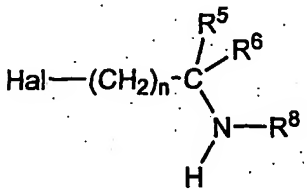
A 2-aryloxyethylbromide is obtained by reacting a hydroxyarene with dibromoethane in aqueous sodium hydroxide (Slyn'ko, N. M.; Tormyshev, V. M. Russ. Journal. Org. Chem. 2000, 36(2), 254-257).



5.1



5.2



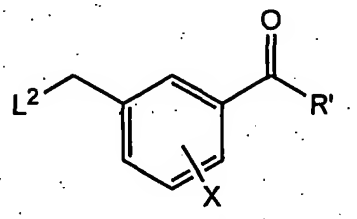
5.3

Alternatively, a primary amine of Formula H_2NR^8, wherein R^8 represents alkyl, cycloalkyl, cyclylalkyl, or arylalkyl, reacts with hereinabove defined dihaloalkane of Formula Hal^1-$(CH_2)_n$-Hal^2 forming a secondary amine of Formula **5.3**, which then is transformed to its respective amide, sulfonamide, carbamate, urethane of Formula **5.1**, wherein R^9 represents alkenylcarbonyl, alkoxycarbonyl, alkylcarbamoyl, alkylcarbonyl, alkylsulfonyl, arylalkenylcarbonyl, arylalkylcarbonyl, arylcarbamoyl, arylcarbonyl, arylalkylsulfonyl, arylsulfonyl, cycloalkylcarbonyl, or cyclylalkylcarbonyl (Briner, K. et. al., Bioorg. Med. Chem. 2002, 10, 3649-3661).

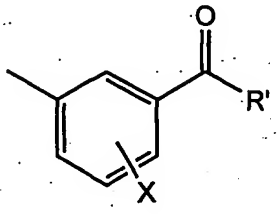
Furthermore, an alkylating reagent of Formula L^2-$(CH_2)_n$-C-$R^5R^6R^7$ can be obtained through transformation of its respective hydroxy analog of Formula $R^5R^6R^7C$-$(CH_2)_n$-OH, by means of known methods.

Especially preferred alkylating reagents, as depicted in Formula **5.4**, **5.5**, **5.4*bis***, are obtained by:

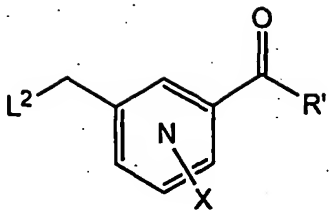
a) halogenation of the methyl group of the benzene and pyridinyl derivatives **6** and **7**, respectively, with known methods, *e.g.* preferably by means of N-X succinimide, whereby X represents halogen, such as chloro or bromo, iodo, in a suitable solvent such as tetrachloromethane, chloroform or the like (de Meijere, A. et al., Chem. Ber. 1993, 126, 1635-1641).



5.4
L^2: Hal (Cl, Br, I)
X: Cl, Br, alkoxy, hydroxyalkoxy
R': alkyl, alkoxy

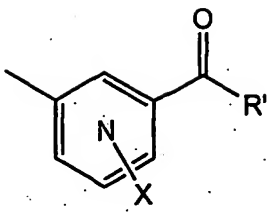


6
X: Cl, Br, alkoxy
R': alkyl, alkoxy



5.5

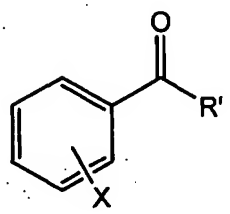
L^2: Hal (Cl, Br, I)
X: Cl, Br
R': alkyl, alkoxy



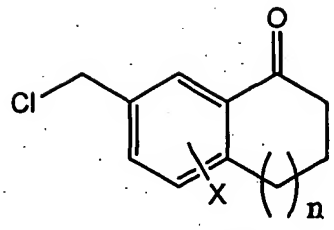
7

X: Cl, Br
R': alkyl, alkoxy

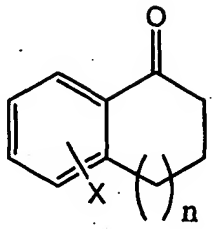
b) direct chloromethylation of the benzene derivatives ***7bis*** or of the bicyclic aromatic compounds ***7ter*** with known methods, *e.g.* preferably by means of methoxyacetyl chloride and aluminium trichloride or a suitable Lewis acid in an polar solvent such as nitromethane, carbon disulfide or the like (McKillop, A.; Madjdabadi, F., A.; Long. D. A. Tetrahedron Lett., 1983, 24, 1933-1936).



7bis
X: alkoxy, hydroxyalkyloxy
R': alkyl, aryl, alkoxy



5.4bis
X: alkoxy, hydroxyalkyloxy
n = 0, 1

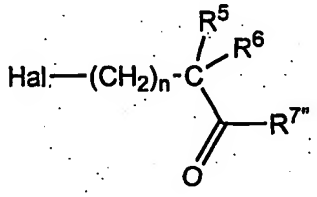


7ter
X: alkoxy, hydroxyalkyloxy
n = 0, 1

In a preferred embodiment, hydroxyalkoxyacetophenone and alkoxyacetophenone ***7bis*** are obtained by alkylation of hydroxyacetophenone with the corresponding

-hydroxyalkyl or alkyl halide (Mandoli, A. *et al* Tetrahedron Asymmetry 2003, 14, 3647-3650).

Another preferred alkyl halide of Formula L^2-$(CH_2)_n$-C-$R^5R^6R^7$ also comprises a structure of Formula **5.6**, wherein $R^{7''}$ represents alkoxy, alkyl-arylamino, arylalkyl-arylamino, or 3,4-dihydro-2*H*-quinoline. Such compounds are obtained by applying methods known to a skilled person.



5.6

Under preferred reaction conditions, a solution of an Intermediate of Formula **3** in acetone is heated at reflux with an alkylating agent of Formula L^2-$(CH_2)_n$-C-$R^5R^6R^7$ in the presence of a base such as potassium carbonate. In case of L^2 representing chloro, or bromo, addition of a catalytic amount of potassium iodide might be beneficial.

Other preferred reaction conditions are those described in:

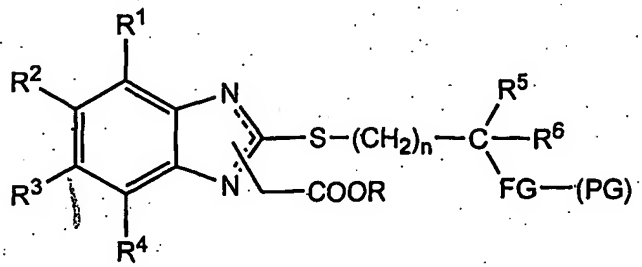
- Yeh, C.-M. and Sun, C.-M. Tetrahedron Lett. 1999, 40, 7247-7250, using alkylbromide in dichloromethane with triethylamine;
- Kühler, T. C. et al., J. Med. Chem. 2002, 45, 4282-4299, using benzylchloride in aqueous sodium hydroxide;
- Matthews, C. et al., J. Chem. Soc., Dalton Trans., 1996, 1531-1538, using alkylhalides in tetrahydrofuran with *N,N*-diisopropyl-ethylamine;
- Terashima, K. et al., Chem. Pharm. Bull 1995, 43, 1985-1991, using alkylbromides with potassium carbonate in *N,N*-dimethylformamide;
- Ram, S. et al., J. Heterocyclic Chem., 1985, 22, 1269-1274, using alkylbromides with potassium carbonate in ethanol or tetrahydrofuran.

In case L^2 in Formula L^2-$(CH_2)_n$-C-$R^5R^6R^7$ represents hydroxy, an alternative method can be applied for the alkylation of an Intermediate of Formula **3**, following typical

Mitsunobu reaction conditions: a compound of Formula **3** reacts with an optionally substituted hydroxyalkyl of Formula $R^5R^6R^7C\text{-}(CH_2)_n\text{-}OH$ in the presence of a trialkyl-, or triaryl-phosphane, and a dehydrating agent, such as a dialkyl azodicarboxylate, particularly di-*tert*-butyl azodicarboxylate, in a suitable solvent, such as toluene, or tetrahydrofurane.

Particularly preferred are hydroxyalkyl of Formula $R^5R^6R^7C\text{-}(CH_2)_n\text{-}OH$, whereby R^5 represents hydrogen, R^6 and R^7 together with the carbon atom to which they are attached form a 4-, 5- or 6-membered heterocyclic ring, containing one nitrogen atom, such as azetidinyl, pyrrolidinyl, or piperidinyl, respectively. Examples are alkylcarbonyl-3-hydroxymethyl-piperidine; alkyloxycarbonyl-3-hydroxymethyl-piperidine, such as *tert*-butyloxycarbonyl-3-hydroxymethyl-piperidine; arylcarbonyl-3-hydroxymethyl-piperidine; alkylsulfonyl-3-hydroxymethyl-piperidine, arylsulfonyl-3-hydroxymethyl-piperidine, arylalkyloxycarbonyl-3-hydroxymethylazetidine, and arylalkylcarbonyl-2-hydroxymethylazetidine.

An Intermediate of Formula **3** can also be alkylated to yield a compound of Formula **4.1**, with a reagent of Formula $L^2\text{-}(CH_2)_n\text{-}C\text{-}R^5R^6R^7$, wherein either one, *e.g.* R^7, of the substituents R^5, R^6, or R^7, is representing a functional group (FG), opted for further transformations. Such functional groups include carboxy; halo, such as chloro or bromo; hydroxyl; and amino. Preferably, a FG group such as amino is introduced in its protected form using a standard protecting group (PG) such as *tert*-butoxycarbonyl, benzyloxycarbonyl, or phthaloyl. Prior to further modifications, PG might be removed by means of standard methods.



4.1 FG = -COOH, Cl, Br, I, OH, NH_2
PG = protecting group

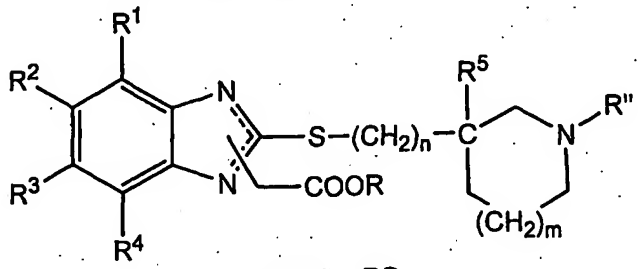
A compound of Formula **4.1** bearing a FG such as carboxy can be transformed to alkoxycarbonyl, N-alkyl-N-arylalkyl-carbamoyl, N-aryl-N-arylalkyl-carbamoyl, N-alkyl-N-aryl-carbamoyl, by means of methods known to a skilled person.

A FG such as halo can be transformed to aryloxy, heterocyclyloxy; or an amino of hereinabove defined Formula NR^8R^9, by means of known methods.

A FG such as hydroxy can be converted to aryloxy, heterocyclyloxy; or an amino of hereinabove defined Formula NR^8R^9, by means of known functional group transformations.

A FG such as amino (NH_2) can be converted stepwise to an amino of hereinabove defined Formula NR^8R^9. Preferred modifications of the nitrogen atom include acylation, alkoxycarbonylation, carbamoylation, or sulfonylation, applying standard conditions.

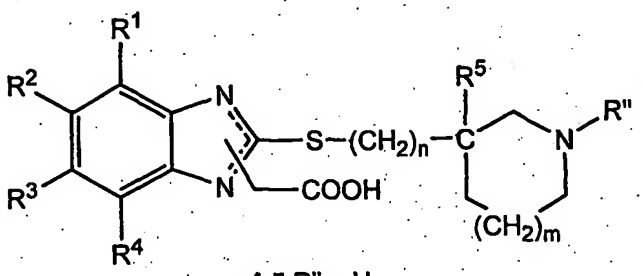
In a preferred embodiment, R^5 in a compound of Formula 4 represents hydrogen, and R^6 and R^7 are forming a pyrrolidine, or piperidinyl ring, whereby a protecting group (PG) is appended to the pyrrolidinyl, or piperidinyl nitrogen atom, as depicted in Formula **4.2**. A standard protecting group (PG), like *e.g. tert*-butoxycarbonyl, or benzyloxycarbonyl, is removed by means of standard conditions, yielding a compound of Formula **4.3**. Subsequently, the nitrogen atom is being further modified with hereinabove defined substituent R^{10}, affording a Precursor of Formula **4.4**. Preferred modifications of the nitrogen atom include acylation, alkoxycarbonylation, carbamoylation, or sulfonylation, applying standard conditions.



4.2 R" = PG
4.3 R" = H
4.4 R" = R^{10}

m= 0,1

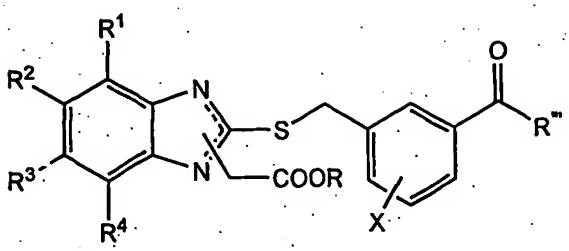
Under the conditions used to remove the protecting group (PG) in a compound of Formula **4.2**, the acetic ester group might be hydrolysed, leading to a compound of Formula **4.5**. In that case, applying a method described for the conversion of a compound of Formula **4.3** to a compound of Formula **4.4** furnishes directly an example of Formula **I-e**.



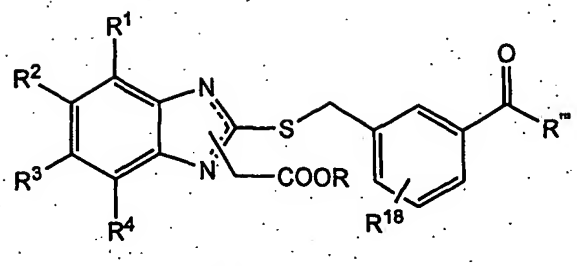
4.5 R" = H
I-e R" = R^{10}

m= 0,1

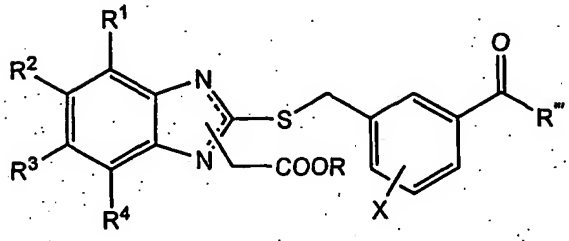
In a preferred embodiment, R^5 and R^6 in a compound of Formula **4** represent hydrogen and R^7 is an aromatic ring bearing two substituents R''' and X as depicted in Formula **4.6**, wherein R''' corresponds to an alkoxy group and X represents a halogen atom such as bromine; or in Formula **4.8** wherein R''' represents hydroxy and X represents an alkyloxy group.



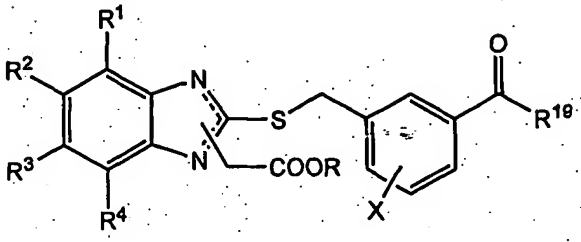
4.6 R''' = alkoxy, X = halogene (Br, Cl, I)



4.7 R''' = alkoxy, X = R^{18}



4.8 R''' = hydroxy, X = alkoxy



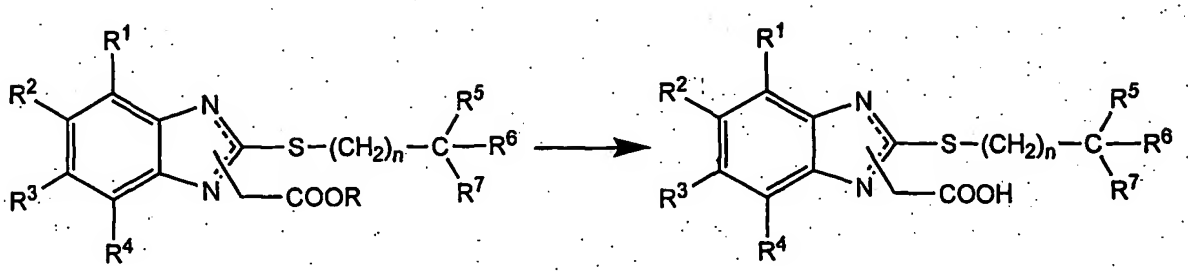
4.9 R''' = R^{19}, X = alkoxy

In the case of a compound of Formula **4.6**, the halogen atom can be replaced by a group R^{18} using standard coupling methods known by a person skilled in the art, for example a Suzuki coupling and yielding a compound as depicted in Formula **4.7**. Examples are compounds were R^{18} represents an aromatic ring such as a phenyl group.

A compound of Formula **4.8**, might be obtained in the typical conditions of a Mitsunobu reaction between an Intermediate of Formula **3** or Formula **3a** and a suitable hydroxymethylbenzoic acid. A compound of Formula **4.8** is subsequently modified so that the hydroxy group R''' is replaced by a primary or secondary amine using standard coupling methods such as with HOBt and EDC (N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide) hydrochloride in a DMF / dichloromethane mixture to yield primary or secondary aromatic amides as depicted in Formula **4.9**. Examples are compounds wherein R^{19} is an indolino-, butylamino-, morpholino-, benzylamino-, diethylamino- or benzylethylamino-group.

Hydrolysis of the ester group R in a Precursor of Formula **4** can be carried out using routine procedures, as outlined in Scheme 2, for example by means of aqueous lithium hydroxide, or sodium hydroxide in an organic solvent such as tetrahydrofuran, dioxane,

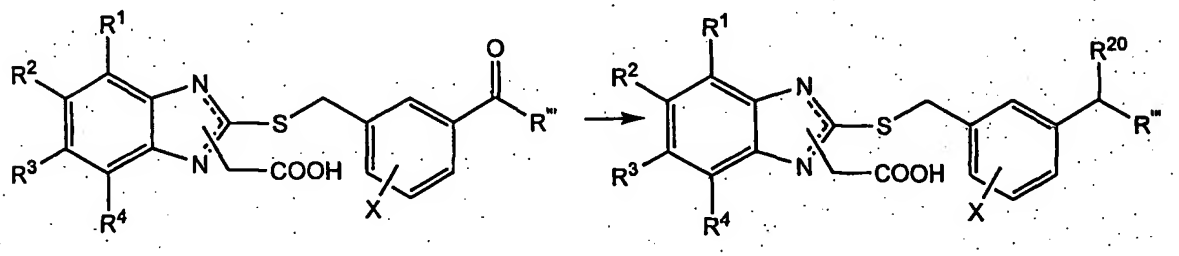
methanol, or with trifluoroacetic acid in dichloromethane to give a compound of Formula **I-a**.



4 **I-a**

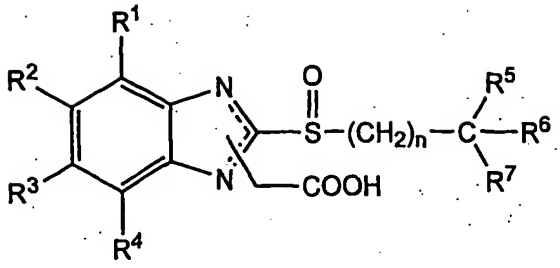
Scheme 2

In a particular case, an example wherein both R^5 and R^6 represent a hydrogen atom and R^7 is an aromatic ring bearing a ketone, as depicted in Formula I-b, can be further modified by a reduction reaction by means of known methods to yield the compound of Formula I-c wherein R^{20} represents hydroxy or alkyloxy. The preferred reaction condition is stirring with sodium borohydride in methanol.



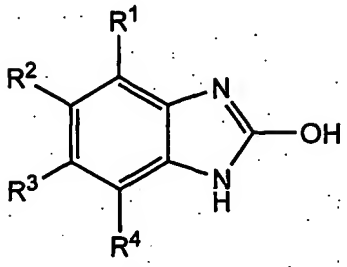
I-b X = alkyloxy, R^{III} =alkyl **I-c** X = alkyloxy, R^{20} = hydroxy, alkoxy

In a preferred embodiment, a compound of Formula I-a can be further oxidized at the sulphur atom by a method known to a person skilled in the art to yield a sulfoxide as depicted in Formula I-d.



I-d

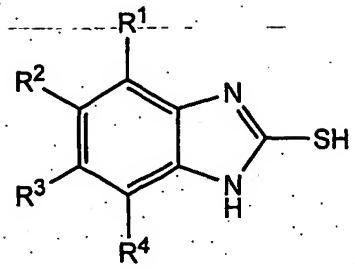
Starting 2-chlorobenzoimidazole of Formula **1** can be prepared from the corresponding 2-hydroxybenzimidazole of Formula **8** by means of phosphorous oxychloride, either neat or in a suitable solvent (Naef, R.; Balli, H., Helv. Chem. Acta 1978, 61, 2958-2973).



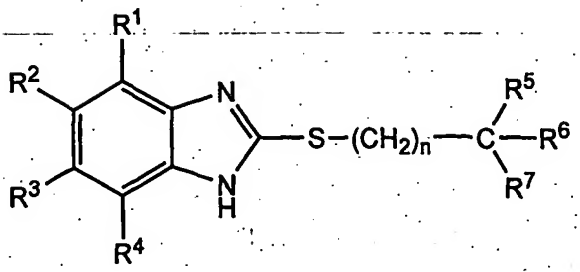
8

2-Chloro-5-nitrobenzimidazole is obtained following a method described in Jung, F.; Delvare, C.; Boucherot, D.; Hamon, A. J. Med. Chem. 1991, 34, 1110-1116.

A Precursor of Formula **4** can also be obtained following a preferred alternative synthetic route, *e.g.* by changing the sequence of reactions. In a first step, starting 1*H*-benzoimidazole-2-thiol of Formula **9** can be *S*-alkylated with hereinabove defined reagent of Formula L^2-$(CH_2)_n$-C-$R^5R^6R^7$ under aforementioned conditions to yield 2-alkylsulfanyl-1*H*-benzoimidazole of Formula **10**, which then is *N*-alkylated in a second step with *tert*-butyl or ethyl bromoacetate to a Precursor of Formula **4**. Any further functional group manipulations, as discussed hereinabove for Intermediates **4.1**, **4.2**, **4.3**, and **4.4**, are preferably accomplished at this stage, prior to ester hydrolysis to the final compound of Formula I.



9



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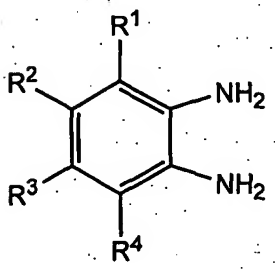
Starting 1*H*-benzoimidazole-2-thiol of Formula **9** is obtained from 1,2-diaminobenzene of Formula **11**, with carbon disulfide, thiocarbonyldiimidazole or potassium xanthogenate in a suitable solvent such as dichloromethane; or an alcohol such as methanol, ethanol, propanol; or water; or a mixture of an alcohol and water; in the presence of a base such as potassium hydroxide, sodium hydroxide, at elevated temperature between 50 and 100°C.



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Preferred reaction conditions are those described in:

- Ikeda, K.; Hata, S.-I.; Tanaka, Y.; Yamamomto, T. OPPI Briefs, 2000, 32, 401-405, using carbondisulfide and potassium hydroxide in a mixture of ethanol and water;
- Kühler, T. C.; Fryklund, J.; Bergman, N.-A.; Weilitz, J.; Lee, A.; Larson, H.; J. Med. Chem, 1995, 38, 4906-4916, using potassium ethylxanthogenate in a mixture of ethanol and water;
- Ram, S.; Wise, D. S.; Townsend, L. B. J. Heterocyclic Chem., 1985, 22, 1269-1274, using potassium ethylxanthogenate and sodium hydroxide in water;
- Wright, J. L.; Gregory, T. F.; Kesten, S. R; Boxer, P. A.; Serpa, K. A.; Meltzer, L.T.; Wise, L. D.; Espitia, S. A.; Konkoy, C. S.; Whittermore, E. R.;

Woodward, R. M.; J. Med. Chem., 2000, 43, 3408-3419 using thiocarbonyldiimidazole in tetrahydrofuran.

Examples

Temperatures are indicated in degrees Celsius (°C). Unless otherwise indicated, the reactions are performed at rt.

In mixtures, relations of parts of solvent or eluent or reagent mixtures in liquid form are given as volume relations (v/v), unless indicated otherwise.

Abbreviations and acronyms used:

AcOEt: ethyl acetate, AcOH: acetic acid, AIBN: 2,2'-azobisisobutyronitrile, $CDCl_3$: deuterochloroform, CCl_4: tetrachlorocarbon, DCE: 1,2-dichloroethane, DBU: 1,8-Diazabicyclo[5.4.0]undec-7-ene, DIPEA: *N,N*-diisopropylethylamine, DMF: *N,N*-dimethylformamide, DMSO-d_6: deuterated dimethyl sulfoxide, DVB: divinyl benzene, eq.: equivalent, ESI: electon spray inonization, Et_3N: triethylamine, Et_2O: diethylether, EtOH: ethanol, g: gram, h: hour, HCl: hydrochloric acid, HOBt: 1-hydroxybenzotriazole, HPLC: high-performance liquid chromatography, k: kilo, KH_2PO_4: potassium phosphate, K_2CO_3: potassium carbonate, l: liter, µ: micro, m: milli, mol: mole, M: molar, MeOH: methanol, Me: methyl, min: minute, $MgSO_4$: magnesium sulfate, MS: mass spectrometry, N: normality of solution, $NaHCO_3$: sodium hydrogencarbonate, Na_2CO_3: sodium carbonate, NaOH: sodium hydroxide, Na_2SO_4: sodium sulfate, NH_4Cl: ammonium chloride, rt: room temperature, $SOCl_2$: thionyl chloride, TFA: trifluoroacetic acid, THF: tetrahydrofuran, t_R: retention time.

Instruments and methods:

-HPLC/MS analyses were performed on a Waters 2795 Alliance HPLC instrument, equipped with a Photodiode Array Detector Waters 996 and a Micromass ZQ™ Waters mass spectrometer (electron spray ionization).

-Analytical HPLC conditions:

LC-1: analytical HPLC on an Xterra™ MS C_{18} column (50 x 2.1 mm, 5µm, Waters), with a linear gradient of water containing 0.06% formic acid (A) and acetonitrile containing 0.06% formic acid (B), from 5% to 95% B over 6 min; flow rate 0.25 ml/min, column temperature 30°C, detection at 200- 400 nm.

LC-2: analytical HPLC on an Xterra™ MS C_{18} column (50 x 4.6 mm, 5µm, Waters), with a linear gradient of water containing 0.06% formic acid (A) and acetonitrile containing 0.06% formic acid (B), from 5% to 95% B over 2 min; flow rate 0.75 ml/min, column temperature 30°C, detection at 200- 400 nm.

LC-3: analytical HPLC on an Zorbax SB-Aq™ column (50 x 4.6 mm, 5µm, Agilent), with a linear gradient of water containing 0.06% formic acid (A) and acetonitrile containing 0.06% formic acid (B), from 5% to 95% B over 1 min; flow rate 3 ml/min, column temperature 30°C, detection at 200- 400 nm.

-Preparative HPLC conditions:

Separations and purifications of compounds on a preparative scale are performed on Waters HPLC system, equipped with a Waters 600 controller, a Waters Preparative Xterra™ Prep MS C_{18} column (19 x 50 mm, 5µm, a Waters 2767 sample manager, a Waters 996 Photodiode Array Detector, and a Micromass ZQTM Waters mass spectrometer (electron spray ionization), with a gradient of water containing 0.825% formic acid (A) and acetonitrile containing 0.825% formic acid (B) from 5% to 95% B over 13 min; flow rate 20 ml / min, column temperature 30°C, detection at 200-400 nm.

-^{1}H NMR spectra were recorded on a Varian Mercury 300VX FT-NMR spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) downfield by reference to proton resonances resulting from incomplete deuteration of the NMR solvent, *e.g.* for dimetylsulfoxide δ(H) 2.49 ppm, for chloroform δ(H) 7.24 ppm.

Syntheses of Intermediates of Formula 3:

Intermediate **3-I**

tert-Butyl-(2-mercapto-benzoimidazol-1-yl) acetate

According to the procedure described in: Migawa, M. T.; Girardet, J.-L.; Walker II, J. A.; Koszalka, G. W.; Chamberlain, S. D.; Drach, J. C.; Townsend, L. B., J. Med. Chem. 1998, 41, 1242-1251, a solution of *tert*-butyl (2-chloro-benzoimidazol-1-yl)-acetate (Intermediate **2-I**, 7 g, 26.3 mmol) and thiourea (7.98 g, 105 mmol) in methanol (100 ml) is refluxed for 2 h. The mixture is cooled down and most of the methanol is removed *in vacuo*. After addition of saturated aqueous NH_4Cl solution (150 ml), the resulting aqueous phase is extracted three times with Et_2O. The combined organic phases are washed with brine and dried over Na_2SO_4. The solvent is evaporated *in vacuo* and the residue dried under high *vacuum*, yielding the title compound (6.46 g) in 93% as a white powder: t_R = 6.14 min (LC-1), ESI-MS (neg.): m/z 263.31 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.50 (s, 9H, *t*Bu), 4.94 (s, 2H, CH_2CO_2), 6.99-7.05 (m, 1 H_{arom}), 7.16-7.24 (m, 1 H_{arom}), 10.69 (bs, 1H, SH).

Intermediate **3-IIa** and Intermediate **3-IIb** of the following Table 3 are prepared from a (1:1) mixture of *tert*-butyl (2-chloro-5-nitro-benzoimidazol-1-yl)-acetate (Intermediate **2-IIa**) and its 6-nitro regioisomer (Intermediate **2-IIb**) analogous to the procedure described for Intermediate **3-I**. They are purified and separated by flash-chromatography on silica-gel (AcOEt / heptane, 1:5).

Intermediate	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
3-IIa	*tert*-Butyl (2-mercapto-5-nitro-benzoimidazol-1-yl)-acetate	C13H15N3O4S 309.34	2.16 (LC-2)	n/a	308.32
3-IIb	*tert*-Butyl (2-mercapto-6-nitro-benzoimidazol-1-yl)-acetate	C13H15N3O4S 309.34	2.16 (LC-2)	n/a	308.32

Table 3

Syntheses of Intermediates of Formula **2**:

Intermediate **2-I**

tert-Butyl (2-chloro-benzoimidazol-1-yl)-acetate

In a round bottomed flask are added K_2CO_3 (9.34 g, 67.7 mmol), 2-chlorobenzimidazole (5.16 g, 33.8 mmol) and *tert*-butyl bromoacetate (6.6 g, 5 ml, 33.8 mmol) in acetone (100 ml). The resulting suspension is refluxed for 1 h. The crude mixture is filtered through a filter paper and water (100 ml) is added. The resulting aqueous phase is extracted three times with Et_2O. The combined organic phases are washed with brine and dried over $MgSO_4$ .The solvent is evaporated under reduced pressure yielding the title compound (7.98 g) in 88% as a white powder: t_R = 2.20 min (LC-2), ESI-MS (pos.): m/z 267.2 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.48 (s, 9H, *tBu*), 4.92 (s, 2H, CH_2CO_2), 7.24-7.40 (m, $3H_{arom}$), 7.76-7.80 (m, $1H_{arom}$).

Intermediate **2-IIa** and **2-IIb**

tert-Butyl (2-chloro-5-nitro-benzoimidazol-1-yl)-acetate and its 6-nitro regioisomer are prepared according to the same procedure (yield 93%): t_R = 6.68 min (LC-1), ESI-MS (pos.): m/z 312.08 $[M+H]^+$, 310.28 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.50 (s, 9H, *t*Bu), 1.52 (s, 9H, *t*Bu), 5.04 and 5.06 (s, 2H, CH_2CO_2), 7.38 (d, 1 H_{arom}), 7.86 (d, 1 H_{arom}), 8.32-8.40 (m, 3 H_{arom}), 8.96 (m, 1 H_{arom}).

Example A-01a

[2-(2-Cyclohexyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid

A solution of *tert*-butyl [2-(2-cyclohexyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetate (Precursor A-01b, 42 mg, 0.13 mmol) in TFA / dichloromethane (1:1, 0.5 ml) is stirred at rt for 4 h. The solvents are removed *in vacuo*. The crude residue is sonicated in Et_2O / heptane (1:1, 1 ml) until a solid precipitates. It is rinsed with heptane and purified by flash chromatography on silica gel (AcOEt / heptane, 1:1 containing 1% of AcOH), yielding the title compound (12 mg) in 30% as a white solid: t_R = 6.44 min (LC-1), ESI-MS (pos.): m/z 319.12 $[M+H]^+$, ESI-MS (neg.): m/z 317.37 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 0.82-0.94 (m, 2H), 1.09-1.23 (m, 3H), 1.37 (m, 1H), 1.54 (q, 2H,

$SCH_2C\underline{H_2}$), 1.68 (m, 5H), 3.34 (t, 2H, SCH_2), 4.88 (s, 2H, CH_2CO_2), 7.22 (s, 3 H_{arom}), 7.65 (m, 1 H_{arom}).

Examples A-02a to A-05a of the following Table 1 are prepared analogous to the procedure described for Example A-01a, using Precursors A-02b to A-05b in place of A-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^-$
A-02a	(2-Hexylsulfanyl-benzoimidazol-1-yl)-acetic acid	C15H20N2O2S 292.402	6.02 (LC-1)	293.27	291.35
A-03a	(2-Pentylsulfanyl-benzoimidazol-1-yl)-acetic acid	C14H18N2O2S 278.375	5.55 (LC-1)	279.08	277.31
A-04a	(2-But-3-enylsulfanyl-benzoimidazol-1-yl)-acetic acid	C13H14N2O2S 262.332	4.69 (LC-1)	263.1	261.28
A-05a	(2-Butylsulfanyl-benzoimidazol-1-yl)-acetic acid	C13H16N2O2S 264.348	4.9 (LC-1)	265.28	263.23

Table 1

Precursor A-01b

tert-Butyl [2-(2-cyclohexyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetate

To a suspension of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 53 mg, 0.2 mmol) and K_2CO_3 (41.4 mg, 0.4 mmol) in acetone (0.8 ml) is added 2-cyclohexylethyl bromide (28.8 mg, 22.6 µl). The reaction mixture is kept stirring at reflux for 5 h then filtered on a short plug of silica gel. The solvents are evaporated and the crude is purified by preparative HPLC yielding the title compound in 60% as a colourless oil: t_R = 7.39 min (LC-1), ESI-MS (pos.): m/z 321.36 $[M+H]^+$; ^1H NMR ($CDCl_3$): δ (ppm) 0.80-0.91 (m, 2H), 1.04-1.23 (m, 3H), 1.35 (s, 9H, *t*Bu), 1.35 (m, 1H), 1.54-1.72 (m, 6H), 1.83 (br. s, 1H), 3.32 (t, 2H, SCH_2), 4.65 (s, 2H, CH_2CO_2), 7.07-7.17 (m, 3 H_{arom}), 7.61 (m, 1 H_{arom}).

Precursors A-02b to A-05b of the following Table 2 are prepared using a procedure analogous to that described for Precursor A-01b, substituting the appropriate alkyl halide for 2-cyclohexylethyl bromide.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
A-02b	*tert*-Butyl (2-hexylsulfanyl-benzoimidazol-1-yl)-acetate	C19H28N2O2S 348.51	7.99 (LC-1)	349.41
A-03b	*tert*-Butyl (2-pentylsulfanyl-benzoimidazol-1-yl)-acetate	C18H26N2O2S 334.48	7.63 (LC-1)	335.35
A-04b	*tert*-Butyl (2-but-3-enylsulfanyl-benzoimidazol-1-yl)-acetate	C17H22N2O2S 318.44	7.04 (LC-1)	319.33
A-05b	*tert*-Butyl (2-butylsulfanyl-benzoimidazol-1-yl)-acetate	C17H24N2O2S 320.46	7.39 (LC-1)	321.36

Table 2

Example B-01a

rac [2-(1-Phenyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid

A solution of rac *tert*-butyl [2-(1-phenyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetate (Precursor B-01b, 46.5 mg, 0.13 mmol) is dissolved in TFA / dichloromethane (1:1, 4.0 ml) and stirred at rt for 3 h. The volatiles are removed *in vacuo* and the residue is dried under high *vacuum*, affording the title compound (26.7 mg) as a yellow oil in 67% yield: t_R = 5.50 min (LC-1), MS (pos.): m/z 313.03 $[M+H]^+$, MS (neg.): m/z 311.16 $[M-H]^+$; ^{1}H NMR (DMSO-d_6): δ (ppm) 1.72 (d, 2H, $CHCH_3$), 4.76 (s, 2H, CH_2CO_2), 5.03 (m, 2H, SCH_2), 7.10 (m, 2 H_{arom}), 7.23-7.32(m, 3 H_{arom}), 7.36 (m, 3 H_{arom}), 7.54 (m, 1 H_{arom}).

Examples B-02a to B-05a of the following Table 4 are prepared analogous to the procedure described for Example B-01a, using Precursors B-02b to B-05b in place of B-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
B-02a	(2-Cyclopentylsulfanyl-benzoimidazol-1-yl)-acetic acid	C14H16N2O2S 276.359	4.7 (LC-1)	n/a	275.19
B-03a	rac [2-(1-Methyloxycarbonyl-1-phenyl-methylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C18H16N2O4S 356.401	5.79 (LC-1)	356.99	355.13
B-04a	rac [2-(Bicyclo[4.2.0]octa-1,3,5-trien-7-ylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C17H14N2O2S 310.376	5.65 (LC-1)	312.34	309.14
B-05a	rac [2-(1-Methyl-2-oxo-2-phenyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C18H16N2O3S 340.402	5.7 (LC-1)	n/a	339.15

Table 4

Precursor B-01b

tert-Butyl [2-(1-phenyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetate

A mixture of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 50 mg, 0.19 mmol), 1-bromomethyl-benzene (38.5 mg, 28.5 µl, 0.2 mmol) and K_2CO_3 (52 mg, 0.38 mmol) in acetone (3 ml) is stirred at reflux overnight. The suspension is cooled to rt and filtered through Celite. Evaporation of the solvent *in vacuo* and drying under high *vacuum* yields quantitatively the title compound as a slightly yellow oil. This material is used in the next step without further purification. t_R = 7.45 min (LC-1), MS (pos.): m/z 369.21 $[M+H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.36 (s, 9H, *t*Bu), 1.73 (d, 3H, Me), 4.94 (m, 2H, CH_2CO_2), 5.09 (q, 1H, SCHMePH), 7.16-7.20 (m, 2 H_{arom}), 7.26-7.36 (m, 3 H_{arom}), 7.44-7.50 (m, 3 H_{arom}), 7.61 (m, 1 H_{arom}).

Precursors B-02b to B-05b of the following Table 5 are prepared using a procedure analogous to that described for Precursor B-01b, substituting the appropriate alkyl halide for 1-bromomethyl-benzene.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^-$
B-02b	*tert*-Butyl (2-cyclopentylsulfanyl-benzoimidazol-1-yl)-acetate	C18H24N2O2S 332.46	7.24 (LC-1)	333.18	n/a
B-03b	rac *tert*-Butyl [2-(1-methyloxycarbonyl-1-phenyl-methylsulfanyl)-benzoimidazol-1-yl]-acetate	C22H24N2O4S 412.5	7.25 (LC-1)	413.16	411.19
B-04b	*tert*-Butyl [2-(bicyclo[4.2.0]octa-1,3,5-trien-7-ylsulfanyl)-benzoimidazol-1-yl]-acetate	C21H22N2O2S 366.48	7.51 (LC-1)	367.14	n/a
B-05b	*tert*-Butyl [2-(1-methyl-2-oxo-2-phenyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetate	C22H24N2O3S 396.5	7.39 (LC-1)	397.13	395.23

Table 5

Example C-01a

[2-(2-Methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid

A solution of *tert*-butyl [2-(2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetate (Precursor C-01b, 20 mg, 0.05 mmol) is stirred in TFA / dichloromethane (1:1, 4.0 ml) at rt overnight. The volatiles are removed *in vacuo* and and the residue is dried under high *vacuum*, yielding the title compound (16.0 mg) in 94 % as a white solid: t_R = 5.27 min (LC-1), MS (pos.): m/z 329.22 $[M+H]^+$, MS (neg.): m/z 327.20 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 3.82 (s, 3H, OCH_3), 4.51 (s, 2H, SCH_2), 4.92 (s, 2H, CH_2CO_2), 6.89 (t, 1 H_{arom}), 7.04 (d, 1 H_{arom}), 7.18 (m, 2 H_{arom}), 7.30 (t, 1 H_{arom}), 7.40 (d, 1 H_{arom}), 7.50 (m, 1 H_{arom}), 7.61 (m, 1 H_{arom}).

Examples C-02a to C-05a of the following Table 6 are prepared analogous to the procedure described for Example C-01a, using Precursors C-02b to C-05b in place of C-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
C-02a	(2-Benzylsulfanyl-benzoimidazol-1-yl)-acetic acid	C16H14N2O2S 298.365	5.37 (LC-1)	299.21	297.22
C-03a	(2-Phenethylsulfanyl-benzoimidazol-1-yl)-acetic acid	C17H16N2O2S 312.392	5.51 (LC-1)	313.09	311.22
C-04a	[2-(3-Phenyl-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C18H18N2O2S 326.419	5.9 (LC-1)	327.06	325.26
C-05a	[2-(3,3-Diphenyl-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C24H22N2O2S 402.517	6.7 (LC-1)	403.2	401.26

Table 6

Precursor C-01b

tert-Butyl [2-(2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetate

A suspension of K_2CO_3 (31.4 mg, 0.23 mmol) in acetone (3 ml) containing *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 30 mg, 0.11 mmol) and 2-methoxybenzyl chloride (17.8 mg, 15.8 µl, 0.11 mmol) is stirred at rt overnight. Filtration over Celite and evaporation of the solvent *in vacuo* affords the pure title compound (27 mg) in 62% yield as a yellow oil: t_R = 7.47 min (LC-1), MS (pos.): m/z 385.20 $[M+H]^+$; ^1H NMR (DMSO-d_6): δ (ppm) 1.37 (s, 9H, *t*Bu), 3.90 (s, 3H, OCH_3), 4.53 (s, 2H, SCH_2), 4.92 (s, 2H, CH_2CO_2), 6.87 (t, 1 H_{arom}), 7.03 (d, 1 H_{arom}), 7.21 (m, 2 H_{arom}), 7.28 (t, 1 H_{arom}), 7.40 (d, 1 H_{arom}), 7.50 (m, 1 H_{arom}), 7.64 (m, 1 H_{arom}).

Precursors C-02b to C-05b of the following Table 7 are prepared using a procedure analogous to that described for Precursor C-01b, substituting the appropriate benzyl halide for 2-methoxybenzyl chloride.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
C-02b	*tert*-Butyl (2-benzylsulfanyl-benzoimidazol-1-yl)-acetate	C20H22N2O2S 354.47	7.27 (LC-1)	355.36
C-03b	*tert*-Butyl (2-phenethylsulfanyl-benzoimidazol-1-yl)-acetate	C21H24N2O2S 368.5	7.46 (LC-1)	369.35
C-04b	*tert*-Butyl [2-(3-phenyl-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C22H26N2O2S 382.52	2.62 (LC-2)	383.31
C-05b	*tert*-Butyl [2-(3,3-diphenyl-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C28H30N2O2S 458.62	8.17 (LC-1)	459.42

Table 7

Example D-01a

{2-[2-(4-Chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid

A solution *tert*-butyl {2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate (Precursor D-01b, 33 mg, 0.79 mmol) is stirred in TFA / dichloromethane (1:1, 0.8 ml) at rt for 3 h. The volatiles are removed *in vacuo* and the residue is purified by flash-chromatography on silica gel (AcOEt / heptane, 1:1; then pure AcOEt), yielding the title compound (27 mg) in 95% as a white solid: t_R = 5.73 min (LC-1), MS (pos.): m/z 362.8 $[M+H]^+$, MS (neg.): m/z 360.8 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 3.88 (m, 2H, SCH_2), 4.22 (t, 2H, OCH_2), 4.88 (s, 2H, CH_2CO_2), 6.54 (d, 2H, H_{arom}), 7.12 (d, 2 H_{arom}), 7.32-7.46 (m, 3 H_{arom}), 7.82 (m, 1 H_{arom}).

Examples D-02a to D-07a of the following Table 8 are prepared analogous to the procedure described for Example D-01a, using Precursors D-02b to D-07b in place of D-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
D-02a	[2-(2-Phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C17H16N2O3S 328.392	5.68 (LC-1)	329.23	327.24

D-03a	{2-[2-(Naphthalen-1-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C21H18N2O3S 378.451	6.39 (LC-1)	379.26	377.34
D-04a	{2-[2-(Naphthalen-2-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C21H18N2O3S 378.451	6.43 (LC-1)	379.26	377.28
D-05a	[2-(3-Phenoxy-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C18H18N2O3S 342.418	5.81 (LC-1)	343.27	341.22
D-06a	(2-{3-[(1-Ethyloxycarbonyl-indazol-3-yl)-oxy]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C22H22N4O5S 454.506	2.44 (LC-2)	453.26	455.11
D-07a	[2-(4-Phenoxy-butylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C19H20N2O3S 356.445	6.02 (LC-1)	357.19	355.21

Table 8

Precursor D-02b

tert-Butyl [2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetate

A mixture of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 53 mg, 0.2 mmol), 1-(2-bromo-ethoxy)-benzene (48.3 mg, 0.22 mmol) and K_2CO_3 (41.4 mg, 0.3 mmol) in acetone (0.8 ml) is refluxed for 3 h. The suspension is cooled to rt and filtered through a short pad of silica-gel. The volatiles are removed *in vacuo* and the residue is dried under high *vacuum* affording the title compound as a colourless oil. This material was used in the next step without further purification: t_R = 2.55 min (LC-2), MS (pos.): m/z 385.2 $[M+H]^+$; ^{1}H NMR ($CDCl_3$): δ (ppm) 1.48 (s, 9H, *t*Bu), 3.96 (m, 2H, SCH_2), 4.48 (t, 2H, OCH_2), 4.90 (s, 2H, CH_2CO_2), 6.90 (d, 2 H_{arom}), 7.24-7.38 (m, 5 H_{arom}), 7.86 (m, 1 H_{arom}).

Precursors D-01b to D-07b of the following Table 9 are prepared using a procedure analogous to that described for Precursor D-02b, substituting the appropriate aryloxyalkylbromide or heterocyclyloxyalkylbromide for (2-bromo-ethoxy)-benzene.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
D-01b	*tert*-Butyl {2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate	C21H24N2O3S 384.49	7.25 (LC-1)	418.66
D-03b	*tert*-Butyl {2-[2-(naphthalen-1-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate	C25H26N2O3S 434.558	7.99 (LC-1)	435.34
D-04b	*tert*-Butyl {2-[2-(naphthalen-2-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate	C25H26N2O3S 434.56	7.94 (LC-1)	435.34
D-05b	*tert*-Butyl [2-(4-phenoxy-butylsulfanyl)-benzoimidazol-1-yl]-acetate	C23H28N2O3S 412.55	2.63 (LC-2)	413.35
D-06b	*tert*-Butyl (2-{3-[(1-ethyloxycarbonyl-indazol-3-yl)-oxy]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C26H30N4O5S 510.61	2.94 (LC-2)	511.24
D-07b	*tert*-Butyl [2-(4-phenoxy-butylsulfanyl)-benzoimidazol-1-yl]-acetate	C23H28N2O3S 412.55	7.68 (LC-1)	413.37

Table 9

Preparation of 3-(3-chloro-propoxy)-indazole-1-carboxylic acid ethyl ester (alkylating agent D-06-d) is described in the paragraph relating the preparation of 2-(3-chloro-propyl)-3-oxo-2,3-dihydro-indazole-1-carboxylic acid ethyl ester (alkylating agent G-01d).

Example E-01a

[2-(5-Ethyloxycarbonyl-pentylsulfanyl)-benzoimidazol-1-yl]-acetic acid

A solution of *tert*-butyl [2-(5-ethyloxycarbonyl-pentylsulfanyl)-benzoimidazol-1-yl]-acetate (Precursor E-01b, 44 mg, 0.11 mmol) in TFA / dichloromethane (1:1, 2 ml) is stirred at rt for 3 h. The solvents are removed under a stream of air. The solid residue is suspended in Et_2O (2 ml) and sonicated. Filtration, rinsing with Et_2O and drying under high *vacuum* yields the title compound (32 mg) as a white solid in 85% yield: t_R = 5.33 min (LC-1), ESI-MS (pos.): m/z 351.07 $[M+H]^+$, ESI-MS (neg.): m/z 349.22 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.25 (t, 3H CH_3), 1.44 (s, 9H, *t*Bu), 1.32-1.44 (m, 2H), 1.52-1.70 (m, 4H), 2.24 (t, 2H, $CH_2C{=}O$), 3.24 (t, 2H, SCH_2), 4.10 (q, 2H, OCH_2), 4.15 (br. s, 1H, CO_2H), 4.86 (s, 2H, CH_2CO_2), 7.24 (s, 3 H_{arom}), 7.63 (m, 1 H_{arom}).

Examples E-02a to E-03a of the following Table 10 are prepared analogous to the procedure described for Example E-01a, using Precursors E-02b and E-03b in place of E-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
E-02a	[2-(3-Ethyloxycarbonyl-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C15H18N2O4S 322.384	4.87 (LC-1)	323.25	321.22
E-03a	[2-(4-Ethyloxycarbonyl-butylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C16H20N2O4S 336.411	5.09 (LC-1)	337.12	335.31

Table 10

Precursor E-01b

tert-Butyl [2-(5-ethyloxycarbonyl-pentylsulfanyl)-benzoimidazol-1-yl]-acetate

A mixture of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 52 mg, 0.2 mmol), 6-bromo-hexanoic acid ethyl ester (49 mg, 39 µl, 0.22 mmol) and K_2CO_3 (55 mg, 0.4 mmol) is refluxed in acetone (2 ml) for 5 h and stirred at rt overnight. Evaporation of the solvent *in vacuo* affords a residue that is purified by flash-chromatography on silica-gel (AcOEt / heptane, 25:75), yielding the title compound (55 mg) in 68% as a colourless oil: t_R = 7.24 min (LC-1), ESI-MS (pos.): m/z 407.23 $[M+H]^+$, ESI-MS (neg.) 405.22 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.25 (t, 3H CH_3), 1.44 (s, 9H, *t*Bu), 1.48 (m, 2H), 1.66 (quint., 2H), 1.79 (quint., 2H), 2.30 (t, 2H, $CH_2C{=}O$), 3.38 (t, 2H, SCH_2), 4.10 (q, 2H, OCH_2), 4.73 (s, 2H, CH_2CO_2), 7.17-7.25 (m, 3 H_{arom}), 7.69 (m, 1 H_{arom}).

Precursors E-02b to E-03b of the following Table 11 are prepared using a procedure analogous to that described for Precursor E-01b, substituting the appropriate alkyl bromide for 6-bromo-hexanoic acid ethyl ester.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
E-02b	*tert*-Butyl [2-(3-ethyloxycarbonyl-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C19H26N2O4S 378.49	2.34 (LC-2)	379.36
E-03b	*tert*-Butyl [2-(4-ethyloxycarbonyl-butylsulfanyl)-benzoimidazol-1-yl]-acetate	C20H28N2O4S 392.51	7.04 (LC-1)	393.35

Table 11

Example F-01a

{2-[4-(Methyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetic acid

tert-Butyl {2-[4-(methyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetate (Precursor F-01b, 25.6 mg, 0.06 mmol) is dissolved in TFA / dichloromethane (1:1, 3 ml) and stirred for 3 h at rt. Evaporation of the solvent *in vacuo* and drying under high *vacuum* yields the title compound (19.4 mg) in 87% as a yellow oil: t_R = 5.20 min (LC-1), ESI-MS (pos.): m/z 398.20 $[M+H]^+$, ESI-MS (neg.): m/z 396.19 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.56 (m, 4H, CH_2CH_2), 2.05 (m, 2H, $CH_2C{=}O$), 3.14 (s, 3H, NMe), 3.22 (m, 2H, SCH_2), 5.00 (s, 2H, CH_2CO_2), 7.18-7.32 (m, 5 H_{arom}), 7.38 (m, 2 H_{arom}), 7.53 (m, 2 H_{arom}).

Examples F-02a to F-05a of the following Table 12 are prepared analogous to the procedure described for Example F-01a, using Precursors F-02b to F-05b in place of F-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
F-02a	{2-[5-(3,4-Dihydro-2*H*-quinolin-1-yl)-5-oxo-pentylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C23H25N3O3S 423.536	5.58 (LC-1)	424.22	422.23

F-03a	{2-[4-(Benzyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C27H27N3O3S 473.595	6.17 (LC-1)	474.17	472.28
F-04a	{2-[4-(benzyl-methyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetic acid;	C22H25N3O3S 411.525	5.31 (LC-1)	412.2	410.16
F-05a	{2-[4-(Butyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C24H29N3O3S 439.578	6.13 (LC-1)	440.17	438.28

Table 12

Precursor F-01b

tert-Butyl {2-[4-(methyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetate

To a suspension of 5-bromovaleryl chloride (24.8 mg, 16.6 µl, 0.12 mmol) and K_2CO_3 (31.2 mg, 0.23 mmol) in acetonitrile (3 ml) is added N-methylaniline (14.5 mg, 14.7 µl, 0.14 mmol). After 1 h of stirring, *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 30 mg, 0.11 mmol) is added and the resulting mixture is refluxed overnight. The crude suspension is filtered over a fritted funnel and the solvent evaporated *in vacuo*. The crude yellow oil is purified by flash-chromatography on silica gel (AcOEt / heptane, 2:1 containing 3% of Et_3N), yielding the title compound (38.4 mg) in 75% as a yellowish oil: t_R = 6.84 min (LC-1), ESI-MS (pos.): m/z 455.46 $[M+H]^+$, ESI-MS (neg.): m/z 452.19 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.38 (s, 9H, *t*Bu), 1.56 (m, 4H, CH_2CH_2), 2.03 (m, 2H, CH_2C=O), 3.17 (m, 2H, SCH_2), 3.31 (s, 3H, NMe), 4.92 (s, 2H, CH_2CO_2), 7.12-7.16 (m, 2 H_{arom}), 7.26-7.30 (m, 3 H_{arom}), 7.36-7.46 (m, 3 H_{arom}), 7.51 (m, 1 H_{arom}).

Precursors F-02b to F-05b of the following Table 13 are prepared using a procedure analogous to that described for Precursor F-01b, substituting the corresponding *N,N*-disubstituted amine for *N*-methylaniline.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z [M-H]+

F-02b	*tert*-Butyl {2-[5-(3,4-dihydro-2*H*-quinolin-1-yl)-5-oxo-pentylsulfanyl]-benzoimidazol-1-yl}-acetate	C27H33N3O3S 479.63	7.23 (LC-1)	481.31	n/a
F-03b	*tert*-Butyl {2-[4-(benzyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetate	C31H35N3O3S 529.69	7.62 (LC-1)	531.43	n/a
F-04b	tert-Butyl {2-[4-(benzyl-methyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetate	C26H33N3O3S 467.62	6.91 (LC-1)	468.08	466.34
F-05b	*tert*-Butyl {2-[4-(butyl-phenyl-carbamoyl)-butylsulfanyl]-benzoimidazol-1-yl}-acetate	C28H37N3O3S 495.68	7.7 (LC-1)	497.44	n/a

Table 13

Example G-01a

{2-[3-(2,3-Dihydro-1-ethyloxycarbonyl-3-oxo-indazol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid

tert-Butyl {2-[3-(2,3-dihydro-1-ethyloxycarbonyl-3-oxo-indazol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate (Precursor G-01b, 63.8 mg, 0.1 mmol) is stirred in TFA / dichloromethane (1:1, 2 ml) at rt overnight. The solvents are removed *in vacuo*. The crude is taken up in chloroform (1 ml) and filtered over cotton wool. The solvent is removed *in vacuuo* and the residue is dried under high *vacuum*. This yields the title compound (6 mg) in 11 % as a colourless oil: t_R = 2.24 min (LC-2), ESI-MS (pos.): m/z 455.11 $[M+H]^+$, ESI-MS (neg.): m/z 453.22 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.31 (t, 3H, CH_3), 2.03 (quint., 2H, CH_2CH_2N), 3.18 (m ,2H, SCH_2), 4.23 (t, 2H, CH_2N), 4.36 (q., 2H, OCH_2), 4.94 (s, 2H, CH_2CO_2), 7.10-7.15 (m, 2 H_{arom}), 7.39 (t, 1 H_{arom}), 7.46 (m, 2 H_{arom}), 7.70-7.78 (m, 2 H_{arom}), 7.87 (d, 1 H_{arom})

Examples G-02a to G-07a of the following Table 14 are prepared analogous to the procedure described for Example G-01a, using Precursors G-02b to G-07b in place of G-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$

G-02a	{2-[3-(1-Oxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C20H19N3O3S 381.455	1.68 (LC-2)	382.43	380.29
G-03a	{2-[3-(2-Oxo-2,3-dihydro-benzoimidazol-1-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C19H18N4O3S 382.443	2.00 (LC-2)	383.19	381.21
G-04a	{2-[3-(1-Oxo-1*H*-phthalazin-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C20H18N4O3S 394.454	2.13 (LC-2)	395.1	393.19
G-05a	{2-[3-(2,4-Dioxo-1,4-dihydro-2*H*-quinazolin-3-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C20H18N4O4S 410.453	1.99 (LC-2)	411.15	409.18
G-06a	{2-[3-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C20H17N3O4S 395.438	5.36 (LC-1)	396.15	394.23
G-07a	{2-[3-(1,1,3-Trioxo-1,3-dihydro-1λ-benzo[d]isothiazol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C19H17N3O5S2 431.492	2.21 (LC-2)	432.05	430.14

Table 14

Precursor G-01b

tert-Butyl {2-[3-(2,3-dihydro-1-ethyloxycarbonyl-3-oxo-indazol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate

A mixture of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 66 mg, 0.25 mmol), 2-(3-chloro-propyl)-3-oxo-2,3-dihydro-indazole-1-carboxylic acid ethyl ester (alkylating agent G-01d, 70 mg, 0.25 mmol), a few crystals of potassium iodide and K_2CO_3 (69 mg, 0.5 mmol) in acetone (1 ml) is refluxed overnight. Evaporation of the solvent under a stream of air affords a residue that is purified by flash-chromatography on silica-gel (AcOEt / heptane, 3:2), yielding the title compound as a colourless oil: t_R = 2.75 min (LC-2), ESI-MS (pos.): m/z 511.15 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.37 (s, 9H, *t*Bu), 1.37 (t, 3H, CH_3), 2.14 (quint., 2H, CH_2CH_2N),

3.28 (m , 2H, SCH_2), 4.30-4.40 (m, 4H), 4.69 (s, 2H, CH_2CO_2), 7.10 (m, 3 H_{arom}), 7.26 (t, 1 H_{arom}), 7.55 (m, 2 H_{arom}), 7.81 (t, 2 H_{arom}).

Precursors G-02b to G-07b of the following Table 15 are prepared using a procedure analogous to that described for Precursor G-01b, substituting the appropriate alkylating agent for G-01d.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
G-02b	*tert*-Butyl {2-[3-(1-oxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C24H27N3O3S 437.55	2.19 (LC-2)	438.29	n/a
G-03b	*tert*-Butyl {2-[3-(2-oxo-2,3-dihydro-benzoimidazol-1-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C23H26N4O3S 438.54	2.67 (LC-2)	439.24	437.27
G-04b	*tert*-Butyl {2-[3-(1-oxo-1*H*-phthalazin-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C24H26N4O3S 450.55	2.67 (LC-2)	451.22	n/a
G-05b	*tert*-Butyl {2-[3-(2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C24H26N4O4S 466.55	2.21 (LC-2)	467.28	465.24
G-06b	*tert*-Butyl {2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C24H25N3O4S 451.55	6.99 (LC-1)	452.40	n/a
G-07b	*tert*-Butyl {2-[3-(1,1,3-trioxo-1,3-dihydro-1λ^6-benzo[d]isothiazol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C23H25N3O5S2 487.59	2.73 (LC-2)	488.17	n/a

Table 15

Alkylating agent G-01d

2-(3-Chloro-propyl)-3-oxo-2,3-dihydro-indazole-1-carboxylic acid ethyl ester

To a solution of 3-oxo-2,3-dihydro-indazole-1-carboxylic acid ethyl ester (410 mg, 2 mmol) dissolved in dry DMF (10 ml) is added sodium hydride (60% w/w in oil, 120 mg, 3 mmol). The resulting cloudy solution is allowed to stir for 1 h at rt and is added dropwise under inert atmosphere via a syringe onto a solution of iodochloropropane

(268 µl, 2.5 mmol) in dry DMF (2 ml). The resulting solution is allowed to stir at rt overnight. By addition of water and evaporation under reduced pressure most of the DMF is removed from the crude mixture. The residue is dissolved in AcOEt (25 ml) and the resulting organic phase is washed 3 times with water and once with brine. The crude product is purified by chromatography on silica gel (AcOEt / heptane, 2:3), yielding the title compound (78 mg) in 15 % as a colourless oil: t_R = 2.17 min (LC-2), ESI-MS (pos.): m/z 283.05 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.38 (t, 3H, CH_3), 2.08 (quint., 2H, $CH_2\underline{CH_2}N$), 3.42 (t, 2H, $C\underline{H_2}Cl$), 4.25 (t, 2H, $NC\underline{H_2}$), 4.39 (q, 2H, $OC\underline{H_2}CH_3$), 7.22 (t, 1 H_{arom}), 7.53 (t, 1 H_{arom}), 7.79 (t, 2 H_{arom}), and 3-(3-chloro-propoxy)-indazole-1-carboxylic acid ethyl ester (125 mg) in 24% as a colourless oil: t_R = 2.49 min (LC-2), ESI-MS (pos.): m/z 283.05 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.44 (t, 3H, CH_3), 2.26 (quint., 2H, $C\underline{H_2}CH_2N$), 3.71 (t, 2H, $C\underline{H_2}Cl$), 4.49 (q, 2H, $OC\underline{H_2}CH_3$), 4.59 (t, 2H, $OC\underline{H_2}CH_2$), 7.20 (t, 1 H_{arom}), 7.46 (t, 1 H_{arom}), 7.59 (d, 1 H_{arom}), 8.02 (d, 1 H_{arom}). 3-(3-Chloro-propoxy)-indazole-1-carboxylic acid ethyl ester is used as alkylating agent D-06d in the preparation of Precursor D-06b.

Alkylating agents G-03d to G-07d of the following Table 16 are prepared using a procedure analogous to that described for alkylating agent G-01d, substituting the appropriate nitrogen containing heterocycle for 3-oxo-2,3-dihydro-indazole-1-carboxylic acid ethyl ester.

Alkylating agent	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
G-03d	1-(3-Chloro-propyl)-1,3-dihydro-benzoimidazol-2-one	C10H11ClN2O 210.66	1.87 (LC-2)	211.11	209.1
G-04d	2-(3-Chloro-propyl)-2*H*-phthalazin-1-one	C11H11ClN2O 222.67	2.02 (LC-2)	223.11	n/a
G-05d	3-(3-Chloro-propyl)-1*H*-quinazoline-2,4-dione	C11H11ClN2O2 238.67	1.9 (LC-2)	239.06	237.05

G-07d	2-(3-Chloro-propyl)-1,1-dioxo-1,2-dihydro-1λ⁶-benzo[d]isothiazol-3-one	C10H10ClNO3S 259.71	2.15 (LC-2)	260.01	n/a

Table 16

Example H-01a

[2-(3-Methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid

A solution of *tert*-butyl [2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetate (Precursor H-01b, 31 mg, 0.075 mmol) in TFA / dichloromethane (1:1, 2 ml) is stirred at rt for 4 h. The solvents are removed under a stream of air. The solid residue is suspended in Et_2O (2 ml) and sonicated. Filtration, rinsing with Et_2O and drying under high *vacuum*, yields the title compound (19.6 mg) in 73% as a white solid: t_R = 5.52 min (LC-1), ESI-MS (pos.): m/z 357.25 $[M+H]^+$, ESI-MS (neg.): m/z 355.29 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 3.83 (s, 3H, OMe), 4.65 (s, 2H, SCH_2), 4.92 (s, 1H, CH_2CO_2), 7.15-7.21 (m, 2 H_{arom}), 7.42-7.48 (m, 2 H_{arom}), 7.57 (m, 1 H_{arom}), 7.72 (d, 1 H_{arom}), 7.81 (d, 1 H_{arom}), 8.05 (s, 1 H_{arom}).

Examples H-02a to H-11a of the following Table 17 are prepared analogous to the procedure described for Example H-01a, using Precursors H-02b to H-11b in place of H-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
H-02a	{2-[(5-Methyloxycarbonyl-pyridin-3-yl)-methylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C17H15N3O4S 357.389	1.68 (LC-2)	358.16	356.18
H-03a	(2-{[(2-Chloro-4-methyloxycarbonyl)-pyridin-6-yl]-methyl-sulfanyl}-benzoimidazol-1-yl)-acetic acid	C17H14N3O4ClS 391.834	5.81 (LC-1)	392.05	390.13

H-04a	{2-[(2-Methyloxycarbonyl-furan-5-yl)-methylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C17H16N2O5S 360.389	5.45 (LC-1)	361.08	359.09
H-05a	{2-[(2-Bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C18H15N2O4BrS 435.297	2.04 (LC-2)	437.02	435.1
H-06a	{2-[(4-Bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C18H15N2O4BrS 435.297	2.06 (LC-2)	436.95	435.1
H-07a	{2-[(5-Bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C18H15N2O4BrS 435.297	2.18 (LC-2)	437.02	435.1
H-08a	{2-[(6-Bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C18H15N2O4BrS 435.297	6.02 (LC-1)	437.05	435.03
H-09a	{2-[(6-Methoxy-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C19H18N2O5S 386.427	1.80 (LC-2)	387.2	385.16
H-10a	[2-(3-Acetyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C18H16N2O3S 340.402	6.48 (LC-1)	341.16	339.14
H-11a	[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C19H18N2O4S 370.428	5.03 (LC-1)	371.06	369.11

Table 17

Precursor H-01b

tert-Butyl [2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetate

A mixture of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 264 mg, 1 mmol), 3-bromomethyl-benzoic acid methyl ester (252 mg, 1.1 mmol) and K_2CO_3 (276 mg, 2 mmol) in acetone (4 ml) is allowed to stir at rt for 2.5 h. The suspension is cooled down to rt and filtered on a funnel filled with cotton wool. Evaporation of the solvent *in vacuo* affords a residue that is purified by flash-

chromatography on silica-gel (AcOEt / heptane, 1:3), yielding the title compound (310 mg) in 75% as a colourless syrup: t_R = 7.19 min (LC-1), ESI-MS (pos.): m/z 413.3 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.42 (s, 9H, *t*Bu), 3.92 (s, 3H, OMe), 4.65 (s, 2H), 4.69 (s, 1H), 7.19-7.26 (m, 3 H_{arom}), 7.36 (t, 1 H_{arom}), 7.59 (d, 1 H_{arom}), 7.73 (m, 1 H_{arom}), 7.92 (d, 1 H_{arom}), 8.06 (s, 1 H_{arom}).

Precursors H-02b to H-11b of the following Table 18 are prepared using a procedure analogous to that described for Precursor H-01b, substituting the appropriate alkylating agent for 5-bromo-hexanoic acid ethyl ester.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
H-02b	*tert*-Butyl {2-[(5-methyloxycarbonyl-pyridin-3-yl)-methylsulfanyl]-benzoimidazol-1-yl}-acetate	C21H23N3O4S 413.49	2.21 (LC-2)	414.21	n/a
H-03b	*tert*-Butyl (2-{[(2-chloro-4-methyloxycarbonyl)-pyridin-6-yl]-methyl-sulfanyl}-benzoimidazol-1-yl)-acetate	C21H22ClN3O4S 447.94	2.78 (LC-2)	448.16	n/a
H-04b	*tert*-Butyl {2-[(2-methyloxycarbonyl-furan-5-yl)-methylsulfanyl]-benzoimidazol-1-yl}-acetate	C21H24N2O5S 416.49	2.41 (LC-2)	417.21	n/a
H-05b	*tert*-Butyl {2-[(2-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-aceate	C22H23BrN2O4S 491.4	2.58 (LC-2)	493.08	n/a
H-06b	*tert*-Butyl {2-[(4-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetate	C22H23BrN2O4S 491.4	2.58 (LC-2)	493.08	n/a
H-07b	*tert*-Butyl {2-[(5-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetate	C22H23BrN2O4S 491.4	2.70 (LC-2)	493.08	n/a
H-08b	*tert*-Butyl {2-[(6-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetate	C22H23BrN2O4S 491.4	2.69 (LC-2)	492.77	n/a
H-09b	*tert*-Butyl {2-[(6-methoxy-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetate	C23H26N2O5S 442.53	2.82 (LC-2)	443.26	n/a

H-10b	*tert*-Butyl [2-(3-acetyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetate	C22H24N2O3S 396.5	8.31 (LC-1)	397.22	395.22
H-11b	*tert*-Butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetate	C25H26N2O4S 426.53	6.86 (LC-1)	427.00	425.14

Table 18

Alkylating agent H-08d

4-Bromo-3-bromomethyl-benzoic acid methyl ester

As described in: Puls, C.; Stolle, A.; de Meijere, A., Chem. Ber. 1992, 1635-1641, and Lew, A.; Chamberlin, A. R., Bioorg. Med. Chem. Lett., 1999, 9, 3267-3272.

A solution of 4-bromo-3-methyl-benzoic acid methyl ester (1 g, 4.37 mmol) and *N*-bromosuccinimide (855 mg, 4.8 mmol) in CCl_4 (5 ml) is refluxed for 2 h. AIBN (20 mg, 0.12 mmol, 3%) is added and the mixture is refluxed for 2 h. This process is repeated twice and the reaction mixture is refluxed overnight. The solvent is evaporated and the yellow residue purified by chromatography on silica-gel (AcOEt / heptane, 1:9), yielding a (2:1) mixture of the title compound and 4-bromo-3,3-dibromomethyl-benzoic acid methyl ester as a colourless solid, which is used without further purification in the next step: t_R = 2.31 min (LC-2), ESI-MS (pos.): m/z 308.99 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 3.92 (s, 3H, $OC\underline{H}_3$), 4.60 (s, $C\underline{H}_2Br$), 7.65 (d, 1 H_{arom}), 7.79 (m, 1 H_{arom}), 8.10 (d, 1 H_{arom}).

Alkylating agents H-02d to H-09d of the following Table 19 are prepared using a procedure analogous to that described for alkylating agent H-08d, substituting the corresponding phenyl or pyridyl derivative analogue for 4-bromo-3-methyl-benzoic acid methyl ester.

Alkylating agent	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
H-02d	5-Bromomethyl-nicotinic acid methyl ester	C8H8BrNO2 230.06	1.78 (LC-2)	232.15

H-03d	2-Bromomethyl-6-chloro-isonicotinic acid methyl ester	C8H7BrClNO2 264.50	2.21 (LC-2)	266.08
H-05d	2-Bromo-3-bromomethyl-benzoic acid methyl ester	C9H8Br2O2 307.97	2.31 (LC-2)	308.99
H-06d	2-Bromo-5-bromomethyl-benzoic acid methyl ester	C9H8Br2O2 307.98	2.31 (LC-2)	308.99
H-07d	3-Bromo-5-bromomethyl-benzoic acid methyl ester	C9H8Br2O2 307.99	2.45 (LC-2)	308.99
H-09d	3-Bromomethyl-4-methoxy-benzoic acid methyl ester	C10H11BrO3 259.10	2.62 (LC-2)	259.07

Table 19

Example I-01a

rac [2-(1-Butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid

rac [2-(Piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid hydrochloride (Precursor I-00a, 10 mg, 0.03 mmol) is suspended in dichloromethane (1 ml) and Et_3N (12.88 mg, 16.6 µl, 0.10 mmol) as well as butyryl chloride (3.42 mg, 3.35 µl, 0.04 mmol) are added subsequently. The resulting mixture is stirred for 30 min at rt. Water (1 ml) is then added and the crude acid is extracted twice with dichloromethane. The combined organic phases are washed with brine and dried over Na_2SO_4. Evaporation of the solvent *in vacuo* affords 6 mg of a brown oil. It is suspended in Et_2O (1 ml) and sonicated until a solid forms. This solid is rinsed with ether and dried under *vacuum*, yielding the title compound (5.9 mg) in 55% as a beige solid: t_R = 1.68 min (LC-2), ESI-MS (pos.): m/z 376.25 $[M+H]^+$, ESI-MS (neg.): m/z 374.21 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6, 100°C): δ (ppm) 0.86 (t, 3H, $CH_2C\underline{H}_3$), 1.27-1.44 (m, 2H), 1.54 (td, 2H, $C\underline{H}_2CH_3$), 1.68 (m, 1H), 1.79-1.95 (m, 2H), 2.25 (t, 2H, CH_2C=O), 2.81 (bm, 2H, $SC\underline{H}_2$), 3.32 (d, 2H, $CHC\underline{H}_2N$), 3.65 (bm, 2H, $CH_2C\underline{H}_2N$), 4.97 (s, 2H, CH_2CO_2), 7.18 (m, 2 H_{arom}), 7.44 (m, 1H_{arom}), 7.54 (m, 1 H_{arom}).

Alternatively, Example I-01a is also synthesized starting from *tert*-butyl [2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate (Precursor I-01b): Precursor I-01b (802 mg, 1.86 mmol) is dissolved in TFA / dichloromethane (1:1, 10 ml) and stirred overnight at rt. Evaporation of the solvents *in vacuo* gives an orange oil which is suspended in Et_2O / heptane (1:1, 2 ml) and sonicated. After filtration, thourough rinsing with Et_2O and drying, the title compound (670 mg) is obtained in 96% as a white solid.

Examples I-02a to I-13a of the following Table 20 are prepared analogous to the procedures described for Example I-01a.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
I-02a	rac {2-[1-(2-Methoxy-benzoyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C23H25N3O4S 439.535	1.80 (LC-2)	440.2	438.29
I-03a	rac [2-(1-Phenylacetyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C23H25N3O3S 423.536	1.87 (LC-2)	424.21	422.3
I-04a	rac [2-(1-Cyclohexanecarbonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C22H29N3O3S 415.556	1.96 (LC-2)	416.25	414.34
I-05a	rac {2-[1-(3-Cyclopentyl-propionyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C23H31N3O3S 429.583	2.11 (LC-2)	430.26	428.35
I-06a	rac [2-(1-Diphenylacetyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C29H29N3O3S 499.633	2.16 (LC-2)	500.28	498.3
I-07a	rac [2-(1-Acetyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C17H21N3O3S 347.438	1.51 (LC-2)	348.16	346.25

I-08a	rac [2-(1-Heptanoyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C22H31N3O3S 417.572	2.1 (LC-2)	418.29	416.31
I-09a	rac {2-[1-(3-Chloro-benzoyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C22H22N3O3ClS 443.954	1.97 (LC-2)	444.15	442.24
I-10a	rac {2-[1-(3-Phenyl-propionyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C24H27N3O3S 437.562	1.97 (LC-2)	438.23	436.31
I-11a	rac {2-[1-(Furan-2-carbonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C20H21N3O4S 399.47	1.76 (LC-2)	400.2	398.22
I-12a	rac {2-[1-(Naphthalene-1-carbonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C26H25N3O3S 459.569	1.96 (LC-2)	460.2	458.29
I-13a	rac {2-[1-(4-Bromo-benzoyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C22H22N3O3BrS 488.405	1.99 (LC-2)	490.08	n/a

Table 20

Precursor I-00a

rac [2-(Piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid hydrochloride

To a 2M HCl solution in Et_2O (2 ml) is added rac *tert*-butyl [2-(1-*tert*-butyloxycarbonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate (Precursor I-00b, 36 mg, 0.08 mmol). The mixture is stirred for 4 h at rt. The precipitated solid is filtered and rinsed with Et_2O to yield quantitatively the title compound as a slightly yellow solid.

Precursor I-00b

rac *tert*-Butyl [2-(1-*tert*-butyloxycarbonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate

tert-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 792 mg, 3 mmol), 3-hydroxymethyl-piperidine-1-carboxylic acid *tert*-butyl ester (838 mg, 3.9 mmol) and triphenylphosphane (1021 mg, 3.9 mmol) are dissolved and stirred under inert atmosphere at 0°C in dry THF (20 ml). Di-*tert*-butyl-azodicarboxylate (690 mg, 3 mmol) is added under the same reaction conditions to the solution. The initially deep yellow colour disappears after 10 min. The reaction mixture is slowly allowed to warm up to rt overnight. Evaporation of the solvent *in vacuo* and purification upon two chromatographies on silica gel (AcOEt / heptane, 1:4), provides the title compound (552 mg) in 38% as a colourless syrup: t_R = 7.66 min (LC-1), ESI-MS (pos.): m/z 462.32 $[M+H]^+$; ^{1}H-NMR (DMSO-d_6 at 100°C): δ (ppm) 1.36 (s, 9H, *t*Bu), 1.40 (m, 2H), 1.42 (s, 9H, *t*Bu), 1.58 (m, 1H), 1.75 (m, 1H), 1.85 (m, 1H), 2.85 (m, 2H, SCH_2), 3.24 (m, 2H, NCH_2), 3.67 (m, 1H, NCH_2), 3.86 (m, 1H, NCH_2), 4.96 (m, 2H, CH_2CO_2), 7.14 (m, 2 H_{arom}), 7.46 (m, 1 H_{arom}), 7.53 (m, 1 H_{arom}).

Precursor I-01b

rac *tert*-Butyl [2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate

A suspension of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Precursor 3-I, 1 g, 3.79 mmol), 1-(3-chloromethyl-piperidin-1-yl)-butan-1-one (alkylating agent I-01d, 771 mg, 3.79 mmol) and K_2CO_3 (1.05 g, 7.58 mmol) in acetone (10 ml) is refluxed for 36 h. The crude mixture is filtered over a fritted-funnel and the solvent evaporated *in vacuo*. The resulting brown gum is purificated by column chromatography on silica-gel (AcOEt / heptane, 3:7 to 1:1), yielding the title compound (802 mg) in 49% as a colourless oil: t_R = 2.19 min (LC-1), ESI-MS (pos.): m/z 432.24 $[M+H]^+$.

Alkylating agent I-01d

1-(3-Chloromethyl-piperidin-1-yl)-butan-1-one

A solution of 1-(3-hydroxymethyl-piperidin-1-yl)-butan-1-one (Starting material I-01e, 1.33 g, 7.20 mmol) in dry chloroform (10 ml) is cooled down to 0°C with an ice-water bath. A solution of $SOCl_2$ (1.43 g, 876 µl, 12 mmol) in dry chloroform (10 ml) is added dropwise. The mixture is allowed to stir at reflux for 30 min. The solution is cooled down to rt, $SOCl_2$ (0.48 g, 0.3 ml, 4.1 mmol) is added dropwise and the resulting solution is allowed to stir at reflux for another 30 min. Evaporation of the solvents

under reduced pressure gives a brown liquid which is purified by column chromatography on silica-gel (AcOEt / heptane, 35:65), yielding the title compound (1.15 g) in 78% as a colourless liquid: ^{1}H-NMR ($CDCl_3$): The product is a (1:1) mixture of rotamers: δ (ppm) 0.95 (t, 3H, CH3), 1.33-1.54 (m, 2H), 1.58-1.95 (m, 3H), 1.68 (quint., 1H, $C\underline{H}_2CH_2CH_3$), 2.32 (dd, 2H, CH_2C=O), 2.60 (t, 0.5H), 2.83 (t, 0.5H), 2.99 (m, 2H), 3.36-3.55 (m, 2H), 3.77 (d, 0.5 H), 3.93 (d, 0.5 H), 4.30 (d, 0.5 H), 4.54 (d, 0.5 H).

Starting material I-01e

1-(3-Hydroxymethyl-piperidin-1-yl)-butan-1-one

To a solution of piperidin-3-yl-methanol (2.3 g, 20 mmol) in water (30 ml) is slowly added NaOH (1.2 g, 30 mmol). After total dissolution butyryl chloride (2.15 g, 2.11 ml, 20.2 mmol) is slowly added dropwise. The resulting mixture is allowed to stir overnight at rt. The water phase is extracted three times with dichloromethane. The combined organic phases are washed with brine and dried over Na_2SO_4. The solvents are evaporated *in vacuo* yielding the title compound (2.48 g) in 66% as a colourless oil which solidifies on standing: t_R = 1.52 min (LC-2), ESI-MS (pos.): m/z 208.00 $[M+Na]^+$; ^{1}H-NMR ($CDCl_3$): The product is a (1:1) mixture of rotamers: δ (ppm) 0.92 (t, 3H, CH_3), 1.21 (m, 0.5 H), 1.33-1.52 (m, 2H), 1.57-1.84 (m, 5H), 2.26-2.32 (m, 2H, CH_2C=O), 2.74 (dt, 0.5H), 2.87 (dd, 0.5H), 3.10 (dd, 1H), 3.26 (ddd, 1H), 3.39-3.45 (m, 1.5 H), 3.51-3.59 (m, 1H), 3.91 (dd, 1 H), 4.29 (dt, 0.5 H).

Example J-01a

{2-[3-(*tert*-Butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid

tert-Butyl {2-[3-(*tert*-butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate (Precursor J-01b, 12.7 mg, 0.025 mmol) is suspended in an aqueous 0.2 M NaOH solution (0.67 ml). After addition of THF (1.3 ml) the resulting solution is allowed to stir overnight at rt. It is then treated with 1M aqueous HCl (3.35 ml), water (2 ml) and dichloromethane (3 ml). The phases are separated and the dichloromethane is removed under reduced pressure. Drying under high *vacuum* yields the pure title compound: t_R = 2.12 min (LC-2), ESI-MS (neg.): m/z 470.47 [M-

H]$^+$; ^{1}H-NMR (DMSO-d_6): δ 1.31 (s, 9H, *t*Bu), 1.88 (quint., 2H, $SCH_2C\underline{H_2}$), 2.73 (m, 2H, $C\underline{H_2}Ph$), 3.24 (t, 2H), 3.28-3.36 (m, 4H), 4.94 (s, 2H, CH_2CO_2), 7.13 (m, 5 H_{arom}), 7.23 (t, 2 H_{arom}), 7.42-7.50(m, 2 H_{arom}).

Examples J-02a to J-07a of the following Table 21 are prepared analogous to the procedure described for Example J-01a, using Precursors J-02b to J-07b in place of J-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
J-02a	(2-{3-[*tert*-Butoxycarbonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C28H36N4O4S 524.684	1.78 (LC-2)	525.53	523.62
J-04a	{2-[3-(Benzyl-*tert*-butoxycarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C24H29N3O4S 455.577	2.24 (LC-2)	456.46	454.55
J-05a	{2-[3-(*tert*-Butoxycarbonyl-cyclopropyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C20H27N3O4S 405.517	2.05 (LC-2)	406.38	404.47
J-06a	{2-[3-(*tert*-Butoxycarbonyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C23H27N3O4S 441.55	2.18 (LC-2)	442.38	440.47
J-07a	(2-{3-[*tert*-Butoxycarbonyl-(2,2-diphenyl-ethyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C31H35N3O4S 545.702	2.51 (LC-2)	546.56	544.65

Table 21

Precursor J-01b

tert-Butyl {2-[3-(*tert*-butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate

2-[3-(*tert*-Butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazole (Precursor J-01c, 239 mg, 0.58 mmol), *tert*-butyl bromoacetate (136 mg, 103 µl, 0.70

mmol) and cesium carbonate (227 mg, 0.70 mmol) are dissolved in dry DMF (6 ml) and allowed to stir for 1 h at rt. N-(2-Mercaptoethyl)aminomethyl polystyrene (1.4 mmol/g, 0.5 g, 0.36 mmol) is added and the crude mixture is stirred at rt for 1 h. After filtration and removal of the solvent *in vacuo*, the crude product is diluted in dichloromethane, washed with a 10% aqueous citric acid solution and with a saturated aqueous $NaHCO_3$ solution. The organic phase is dried over $MgSO_4$ and the solvent evaporated *in vacuo*, yielding the title compound: t_R = 2.79 min (LC-2), ESI-MS (neg.): m/z 526.61 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.46 (s, 18H, 2 x *t*Bu), 2.00 (m, 2H, $SCH_2C\underline{H}_2$), 2.85 (m, 2H, $C\underline{H}_2Ph$), 3.26-3.85 (m, 6H), 4.77 (s, 2H, CH_2CO_2), 7.44-7.59 (m, 8 H_{arom}), 7.94 (m, 1 H_{arom}).

Precursors J-02b to J-07b from Table 22 are prepared by a procedure analogous to that described for Precursor J-01b, using Intermediates J-02c to J-07c in place of J-01c.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
J-02b	*tert*-Butyl (2-{3-[*tert*-butoxycarbonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C32H44N4O4S 580.79	2.40 (LC-2)	581.67
J-03b	*tert*-Butyl [2-(3-{[(4-ethyloxycarbonyl)-phenyl]-*tert*-butyloxycarbonyl-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C30H39N3O6S 569.72	2.75 (LC-2)	570.65
J-04b	*tert*-Butyl {2-[3-(benzyl-tert-butoxycarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C28H37N3O4S 511.69	2.73 (LC-2)	512.59
J-05b	*tert*-Butyl {2-[3-(*tert*-butoxycarbonyl-cyclopropyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C24H35N3O4S 461.63	2.62 (LC-2)	462.51
J-06b	*tert*-Butyl {2-[3-(*tert*-butoxycarbonyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C27H35N3O4S 497.66	2.68 (LC-2)	498.57
J-07b	*tert*-Butyl (2-{3-[*tert*-butoxycarbonyl-(2,2-diphenyl-ethyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C35H43N3O4S 601.81	2.89 (LC-2)	602.70

Table 22

Example K-01a

{2-[3-(Butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid

A solution of *tert*-butyl {2-[3-(butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate (Precursor K-01b, 200 mg, 0.38 mmol) is dissolved in TFA / dichloromethane (1:1, 3 ml). The resulting solution is allowed to stir at rt overnight. The solvent is evaporated under reduced pressure and the crude product is triturated in Et_2O (2 ml) until a solid forms. It is filtered, washed thoroughly with Et_2O and dried under high *vacuum*, yielding quantitatively the title compound (179 mg) as a white powder: t_R = 6.82 min (LC-1), ESI-MS (neg.): m/z 470.19 $[M-H]^+$, ESI-MS (neg.): m/z 468.32 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 0.82 (t, 3H, CH_2CH_3), 1.29 (m, 2H, CH_2CH_3), 1.48 (quint., 2H, OCH_2CH_2), 1.71 (m, 2H, SCH_2CH_2), 2.67 (bs, 2H, $PhCH_2$), 3.12 (m, 4H), 3.26 (bs, 2H, $PhCH_2CH_2N$), 3.94 (bs, 2H, OCH_2), 4.77 (s, 2H, CH_2CO_2), 7.05 (s, 2 H_{arom}), 7.08-7.18 (m ,6 H_{arom}), 7.53 (m, 1 H_{arom}).

Alternatively, Example K-01a is synthesized analogous to the procedure described for Example J-01a, using Precursor K-01b in place of J-01b.

Examples K-02a to K-04a of the following Table 23 are prepared analogous to the procedures described for Example K-01a, using Precursors K-02b to K-04b in place of K-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
K-02a	{2-[3-(Benzyl-butoxycarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C24H29N3O4S 455.577	2.28 (LC-2)	456.52	454.61

K-03a	{2-[3-(Butoxycarbonyl-cyclohexyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C23H33N3O4S 447.598	2.39 (LC-2)	448.49	446.58
K-04a	{2-[3-(Butoxycarbonyl-(cyclohexylmethyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C24H35N3O4S 461.625	2.50 (LC-2)	462.57	460.60

Table 23

Precursor K-01b

tert-Butyl {2-[3-(butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate

is generally prepared analogous to the procedure described for Precursor J-01b, using K-01c in place of J-01c.

Alternatively, Precursor K-01b is prepared starting from *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**):

To a suspension of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 290 mg, 1.1 mmol) and K_2CO_3 (304 mg, 2.2 mmol, 2 eq.) in acetone (4 ml) are added (3-chloro-propyl)-phenethyl-carbamic acid butyl ester (alkylating agent K-01d, 387 mg, 1.3 mmol) and a few crystals of potassium iodide. The resulting mixture is allowed to stir at reflux overnight. It is cooled down and filtered on a fritted funnel. Evaporation of the solvent *in vacuo* affords a crude oil that is purified by chromatography on silica gel (AcOEt / heptane, 15:85), yielding the title compound (210 mg) in 36% as a white solid: t_R = 8.25 min (LC-1), ESI-MS (pos.): m/z 526.28 $[M+H]^+$, ESI-MS (neg.): m/z 524.14 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 0.95 (t, 3H, CH_2CH_3), 1.42 (m, 2H, CH_2CH_3), 1.46 (s, 9H, *t*Bu), 1.62 (quint., 2H, OCH_2CH_2), 2.01 (m, 2H, SCH_2CH_2), 2.85 (bs, 2H, $PhCH_2$), 3.34 (m, 2H), 3.45 (m, 2H, $SCH_2CH_2CH_2N$), 4.08 (bs, 2H, OCH_2), 4.74 (s, 2H, CH_2CO_2), 7.14-7.30 (m, 8 H_{arom}), 7.64 (m, 1 H_{arom}).

Precursors K-02b to K-04b in Table 24 are prepared analogous to the procedures described for Precursor K-01b.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
K-02b	*tert*-Butyl {2-[3-(benzyl-butoxycarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C28H37N3O4S 511.68	2.74 (LC-2)	512.59
K-03b	*tert*-Butyl {2-[3-(butoxycarbonyl-cyclohexyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C27H41N3O4S 503.71	2.86 (LC-2)	504.56
K-04b	*tert*-Butyl {2-[3-(butoxycarbonyl-cyclohexylmethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C28H43N3O4S 517.73	2.96 (LC-2)	518.58

Table 24

Intermediate J-01c

2-[3-(*tert*-Butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazole

Phenethyl-carbamic acid *tert*-butyl ester (1107 mg, 5.0 mmol) is dissolved in dry DMF (7.75 ml). To this solution, sodium hydride (60 % w/w in oil, 302 mg, 7.55 mmol) is added under vigorous stirring and stirring is continued for 30 min. Then 1-chloro-3-iodo-propane (250 mg, 5.0 mmol) is dropped into the solution followed by stirring for 2 h at rt and another hour at 50 °C. After switching off the heating and addition of sodium 1*H*-benzoimidazole-2-thiolate (1722 mg, 10 mmol) the mixture is allowed to stir overnight at rt. All the DMF is evaporated *in vacuo* and the remaining crude is dissolved in DCE. This organic phase is washed twice with water, dried over Na_2SO_4 and evaporated to give the crude product which is purified by flash chromatography on silica gel (AcOEt / heptane, 1:9 to 1:1), yielding the title compound (289 mg) in 14% as a colourless oil: t_R = 2.24 min (LC-2), ESI-MS (pos.): m/z 412.43 $[M+H]^+$, MS (neg.): m/z 410.46 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.48 (s, 9H, *t*Bu), 1.89 (br. s, 2H, $SCH_2C\underline{H}_2$), 2.83 (t, 2H, $PhC\underline{H}_2CH_2N$), 3.09 (br. s, 2H), 3.26 (br. s, 1H), 3.42 (t, 2H, $PhCH_2C\underline{H}_2N$), 3.47 (br. s, 2H), 7.13-7.30 (m ,7 H_{arom}), 7.52 (m, 2H).

Intermediates J-02c to J-07c and K-01c to K-04c of the following Table 25 are prepared using a procedure analogous to that described for Intermediate J-01c, substituting the appropriate carbamate or amide for phenethyl-carbamic acid *tert*-butyl ester.

Intermediate	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z [M-H]+
J-02c	2-{3-[*tert*-Butoxycarbonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazole	C26H34N4O2S 466.648	1.84 (LC-2)	467.48	465.50
J-03c	2-(3-{[(4-Ethyloxycarbonyl)-phenyl]-*tert*-butyloxycarbonyl-amino}-propylsulfanyl)-benzoimidazole	C24H29N3O4S 455.577	2.20 (LC-2)	456.46	454.48
J-04c	2-[3-(Benzyl-*tert*-butoxycarbonyl-amino)-propylsulfanyl]-benzoimidazole	C22H27N3O2S 397.541	2.18 (LC-2)	398.38	396.46
J-05c	2-[3-(*tert*-Butoxycarbonyl-cyclopropyl-amino)-propylsulfanyl]-benzoimidazole	C18H25N3O2S 347.482	1.96 (LC-2)	348.42	346.38
J-06c	2-[3-(*tert*-Butoxycarbonyl-phenyl-amino)-propylsulfanyl]-benzoimidazole	C21H25N3O2S 383.514	2.13 (LC-2)	384.40	382.41
J-07c	2-{3-[*tert*-Butoxycarbonyl-(2,2-diphenyl-ethyl)-amino]-propylsulfanyl}-benzoimidazole	C29H33N3O2S 487.666	2.44 (LC-2)	488.44	486.53
K-01c	2-[3-(Butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazole	C23H29N3O2S 411.56	2.23 (LC-2)	412.37	410.52

K-02c	2-[3-(Benzyl-butoxycarbonyl-amino)-propylsulfanyl]-benzoimidazole	C22H27N3O2S 397.53	2.15 (LC-2)	398.43	396.44
K-03c	2-[3-(Butoxycarbonyl-cyclohexyl-amino)-propylsulfanyl]-benzoimidazole	C21H31N3O2S 389.55	2.26 (LC-2)	390.39	388.48
K-04c	2-{3-[Butoxycarbonyl-(cyclohexylmethyl)-amino]-propylsulfanyl}-benzoimidazole	C22H33N3O2S 403.58	2.41 (LC-2)	404.47	402.56

Table 25

Alkylating agent K-01d

(3-Chloro-propyl)-phenethyl-carbamic acid butyl ester

To a solution of phenethyl-carbamic acid butyl ester (3.9 g, 17.64 mmol) in dry DMF (20 ml) cooled to 0°C with an ice-water bath is added sodium hydride (60% w/w in oil, 705 mg, 17.64 mmol). After addition is complete the resulting slurry is allowed to stir at rt for 30 min. It is then cooled down to 0°C again and iodochloropropane (9.0 g, 4.73 ml, 44.1 mmol) is added over 5 min. The slurry is allowed to stir at rt overnight. Water is added until pH=7 and the water phase is extracted twice with AcOEt. The combined organic phases are washed with water / brine (1:1) and dried over $MgSO_4$. The solvent is evaporated *in vacuo* to afford 5 g of a yellow oil containing some DMF. It is purified by flash chromatography on silica-gel (AcOEt / heptane, 1:1), yielding the title compound (1.45 g) in 30% as a colourless oil: t_R = 7.77 min (LC-1), ESI-MS (pos.): m/z 298.18 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 0.96 (t, 3H, CH_3), 1.40 (m, 2H, CH_2CH_2), 1.64 (m, 2H, CH_2CH_2), 1.99 (m, 2H, $C\underline{H}_2CH_2N$), 2.87 (m, 2H, $C\underline{H}_2Ph$), 3.32 (m, 2H, $C\underline{H}_2N$), 3.46-3.53 (m, 4H), 7.16-7.22 (m, 3 H_{arom}), 7.24-7.32 (m, 3 H_{arom}).

Example Q-01a

{2-[3-(Pentanoyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic

A solution of *tert*-butyl {2-[3-(pentanoyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate (Precursor Q-01b, 5.5 mg, 0.01 mmol) in TFA /

dichloromethane (1:1, 1.5 ml) is stirred for 3 h at rt. Toluene (2 ml) is added in the reaction mixture and the solvents are evaporated *in vacuo* yielding the title compound: t_R = 2.17 min (LC-2), ESI-MS (pos.): m/z 454.55 $[M+H]^+$, ESI-MS (neg.): m/z 452.57 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6 at 100°C): δ (ppm) 0.80 (t, 3H, CH_2CH_3), 1.19 (m, 2H, CH_2CH_3), 1.31-1.46 (m, 2H, $CH_2CH_2CH_3$), 1.93 (m, 2H, CH_2CH_2N), 2.09 (m, 1H, $COCH_a$), 2.27 (m, 1H, $COCH_b$), 2.71-2.81 (m, 2H, CH_2Ph), 3.24-3.34 (m, 2H), 3.37-3.51 (m, 4H), 5.01 (m, 2H, CH_2CO_2), 7.15-7.28 (m ,7 H_{arom}), 7.53 (m, 2 H_{arom}).

All the Examples of the following Table 26 are prepared analogous to the procedure described for Example Q-01a, using the appropriate Precursor in place of Q-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
L-01a	{2-[3-(Pentanoyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C23H27N3O3S 425.551	2.15 (LC-2)	426.45	424.54
L-02a	{2-[3-(Diphenylacetyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C32H29N3O3S 535.666	2.40 (LC-2)	536.49	535.64
L-03a	{2-[3-(Phenyl-phenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C26H25N3O3S 459.569	2.13 (LC-2)	460.41	458.56
L-04a	(2-{3-[(3,3-diphenyl-propionyl)-phenyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;	C33H31N3O3S 549.693	2.39 (LC-2)	550.57	548.66
L-05a	{2-[3-(Benzenesulfonyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C24H23N3O4S2 481.596	2.12 (LC-2)	482.45	480.48
L-06a	rac (2-{3-[(2-Cyclohexyl-2-phenyl-acetyl)-phenyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C32H35N3O3S 541.714	2.65 (LC-2)	542.54	540.7
L-07a	{2-[3-(1,3-Diphenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C25H24N4O3S 460.557	2.04 (LC-2)	461.43	459.58

L-08a	{2-[3-(3-Benzyl-1-phenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C26H26N4O3S 474.583	2.02 (LC-2)	475.51	473.53
M-01a	(2-{3-[Pentanoyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C28H36N4O3S 508.685	1.99 (LC-2)	509.53	507.62
M-02a	(2-{3-[Diphenylacetyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C37H38N4O3S 618.8	2.41 (LC-2)	619.66	617.74
M-03a	(2-{3-[Phenylmethanesulfonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C30H34N4O4S2 578.756	1.99 (LC-2)	579.57	577.66
M-04a	(2-{3-[Phenylacetyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C31H34N4O3S 542.702	2.03 (LC-2)	543.56	n/a
M-05a	(2-{3-[(3,3-Diphenyl-propionyl)-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C38H40N4O3S 632.827	2.41 (LC-2)	633.68	631.76
M-06a	(2-{3-[1-(4-Piperidin-1-yl-phenyl)-3-propyl-ureido]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C27H35N5O3S 509.673	1.68 (LC-2)	510.55	508.64
M-07a	(2-{3-[Benzenesulfonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C29H32N4O4S2 564.729	2.01 (LC-2)	565.55	563.57
N-01a	[2-(3-{[(4-Ethyloxycarbonyl)-phenyl]-pentanoyl-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C26H31N3O5S 497.614	2.21 (LC-2)	498.51	496.6
N-02a	[2-(3-{Diphenylacetyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C35H33N3O5S 607.729	2.47 (LC-2)	608.63	606.72

N-03a	(2-{3-[(4-Ethyloxycarbonylphenyl)-(phenylacetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C29H29N3O5S 531.631	2.22 (LC-2)	532.48	530.56
N-04a	[2-(3-{Diphenylpropionyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C36H35N3O5S 621.756	2.45 (LC-2)	622.65	620.67
N-05a	rac [2-(3-{(2-Cyclohexyl-2-phenyl-acetyl)-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C35H39N3O5S 613.777	2.71 (LC-2)	614.62	612.71
O-01a	{2-[3-(Benzyl-pentanoyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C24H29N3O3S 439.578	2.10 (LC-2)	440.47	438.55
O-02a	{2-[3-(Benzyl-diphenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C33H31N3O3S 549.693	2.38 (LC-2)	550.51	548.66
O-03a	{2-[3-(Benzyl-(phenylmethanesulfonyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C26H27N3O4S2 509.649	2.20 (LC-2)	510.43	508.58
O-04a	{2-[3-(Benzyl-(phenylacetyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C27H27N3O3S 473.595	2.11 (LC-2)	474.49	472.58
O-05a	(2-{3-[Benzyl-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C34H33N3O3S 563.72	2.37 (LC-2)	564.59	562.62
O-06a	{2-[3-(1-Benzyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C23H28N4O3S 440.566	1.93 (LC-2)	441.48	439.57
O-07a	{2-[3-(Benzenesulfonyl-benzyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C25H25N3O4S2 495.622	2.20 (LC-2)	496.41	494.5

O-08a	rac (2-{3-[Benzyl-(2-cyclohexyl-2-phenyl-acetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C33H37N3O3S 555.741	2.58 (LC-2)	556.56	554.72
P-01a	{2-[3-(Cyclopropyl-pentanoyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C20H27N3O3S 389.518	1.93 (LC-2)	390.46	388.48
P-02a	(2-{3-[(Butane-1-sulfonyl)-cyclopropyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C19H27N3O4S2 425.572	1.96 (LC-2)	426.39	424.47
P-03a	{2-[3-(Cyclopropyl-diphenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C29H29N3O3S 499.633	2.25 (LC-2)	500.49	498.57
P-04a	{2-[3-(Cyclopropyl-(phenylmethanesulfonyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C22H25N3O4S2 459.589	1.99 (LC-2)	460.41	458.5
P-05a	{2-[3-(Cyclopropyl-(phenylacetyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C23H25N3O3S 423.536	1.94 (LC-2)	424.41	422.5
P-06a	(2-{3-[Cyclopropyl-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C30H31N3O3S 513.66	2.23 (LC-2)	514.51	512.66
P-07a	{2-[3-(1-Cyclopropyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C19H26N4O3S 390.506	1.71 (LC-2)	391.41	389.5
P-08a	{2-[3-(Benzenesulfonyl-cyclopropyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C21H23N3O4S2 445.563	2.06 (LC-2)	446.45	444.48
P-09a	rac (2-{3-[(2-Cyclohexyl-2-phenyl-acetyl)-cyclopropyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C29H35N3O3S 505.681	2.48 (LC-2)	506.60	504.63

Q-02a	(2-{3-[(Butane-1-sulfonyl)-phenethyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C24H31N3O4S2 489.659	2.25 (LC-2)	490.55	488.51
Q-03a	{2-[3-(Diphenylacetyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C34H33N3O3S 563.72	2.42 (LC-2)	564.66	562.62
Q-04a	{2-[3-(phenethyl-(phenylmethanesulfonyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;	C27H29N3O4S2 523.676	2.26 (LC-2)	524.57	522.53
Q-05a	{2-[3-(Phenethyl-(phenylacetyl)amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C28H29N3O3S 487.622	2.17 (LC-2)	488.57	486.53
Q-06a	(2-{3-[(3,3-Diphenyl-propionyl)-phenethyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C35H35N3O3S 577.747	2.42 (LC-2)	578.68	576.64
Q-07a	{2-[3-(1-Phenethyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C24H30N4O3S 454.593	2.00 (LC-2)	455.57	453.53
Q-08a	{2-[3-(Benzenesulfonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C26H27N3O4S2 509.649	2.27 (LC-2)	510.55	508.52
R-01a	(2-{3-[(2,2-Diphenyl-ethyl)-pentanoyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C31H35N3O3S 529.703	2.37 (LC-2)	530.69	528.65
R-02a	(2-{3-[Diphenylacetyl-(2,2-diphenyl-ethyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C40H37N3O3S 639.818	2.59 (LC-2)	640.75	638.71
R-03a	(2-{3-[(2,2-Diphenyl-ethyl)-(phenylmethanesulfonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C33H33N3O4S2 599.774	2.43 (LC-2)	600.66	598.62

R-04a	(2-{3-[(2,2-Diphenyl-ethyl)-(phenylacetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C34H33N3O3S 563.72	2.38 (LC-2)	564.66	562.62
R-05a	(2-{3-[(2,2-Diphenyl-ethyl)-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C41H39N3O3S 653.845	2.58 (LC-2)	654.83	652.73
R-06a	(2-{3-[1-(2,2-Diphenyl-ethyl)-3-propyl-ureido]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C30H34N4O3S 530.691	2.22 (LC-2)	531.65	529.61
T-02a	[2-(3-Pentanoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C17H23N3O3S 349.454	1.62 (LC-2)	350.45	348.42
T-03a	{2-[3-(Butane-1-sulfonylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C16H23N3O4S2 385.508	1.73 (LC-2)	386.44	384.4
T-04a	[2-(3-Diphenylacetylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C26H25N3O3S 459.569	2.05 (LC-2)	460.53	458.56
T-05a	[2-(3-Phenylmethanesulfonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C19H21N3O4S2 419.525	1.78 (LC-2)	420.46	418.42
T-06a	[2-(3-Phenylacetylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C20H21N3O3S 383.471	1.67 (LC-2)	384.47	382.43
T-07a	{2-[3-(3,3-Diphenyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C27H27N3O3S 473.595	2.02 (LC-2)	474.55	472.58
T-08a	{2-[3-(3-Propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C16H22N4O3S 350.442	1.47 (LC-2)	351.47	349.43
T-09a	[2-(3-Benzenesulfonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C18H19N3O4S2 405.498	1.76 (LC-2)	406.44	404.41

T-10a	rac {2-[3-(2-Cyclohexyl-2-phenyl-acetylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C26H31N3O3S 465.616	2.23 (LC-2)	466.65	464.55
T-11a	{2-[3-(3-Phenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C19H20N4O3S 384.459	1.67 (LC-2)	385.49	383.38
T-12a	[2-(3-Benzoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C19H19N3O3S 369.444	2.27 (LC-2)	370.28	368.36
T-13a	{2-[3-(Cyclohexanecarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C19H25N3O3S 375.492	1.75 (LC-2)	376.38	374.39
T-14a	{2-[3-(4-Methoxy-benzoylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C20H21N3O4S 399.47	1.68 (LC-2)	400.31	399.47
T-15a	(2-{3-[(Furan-2-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C17H17N3O4S 359.405	1.51 (LC-2)	360.27	358.29
T-16a	{2-[3-(Cyclopropanecarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C16H19N3O3S 333.411	1.42 (LC-2)	334.29	332.37
T-17a	(2-{3-[(Naphthalene-1-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C23H21N3O3S 419.504	1.88 (LC-2)	420.33	418.40
T-18a	{2-[3-(3-Cyclopentyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C20H27N3O3S 389.518	2.08 (LC-2)	390.36	n/a
T-19a	{2-[3-(2,2-Dimethyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C17H23N3O3S 349.454	1.61 (LC-2)	350.33	348.41
T-20a	{2-[3-(3-Phenyl-acryloylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C21H21N3O3S 395.482	1.80 (LC-2)	396.27	394.41

T-21a	{2-[3-(3-Phenyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C21H23N3O3S 397.498	1.74 (LC-2)	398.32	396.39
T-22a	{2-[3-(1,2-Dioxo-2-ethyloxy-ethylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C16H19N3O5S 365.409	1.50 (LC-2)	366.24	364.32
T-23a	(2-{3-[(Biphenyl-4-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C25H23N3O3S 445.542	2.09 (LC-2)	446.32	444.46
T-24a	(2-{3-[(Pyridine-3-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	C18H18N4O3S 370.432	1.34 (LC-2)	371.31	369.38
T-25a	{2-[3-(3,3-Dimethyl-butyrylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C18H25N3O3S 363.481	1.70 (LC-2)	364.38	362.39
T-26a	[2-(3-Octanoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C20H29N3O3S 391.534	2.03 (LC-2)	392.42	390.43
T-27a	{2-[3-(4-Bromo-benzoylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C19H18BrN3O3S 448.34	1.90 (LC-2)	450.23	448.31

Table 26

Precursor Q-01b

tert-Butyl {2-[3-(pentanoyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate

[3-(1-*tert*-Butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-phenethyl-ammonium chloride (Precursor U-01b, 11.6 mg, 0.025 mmol) and Et_3N (12.2 mg, 17.2 µl, 0.1 mmol) are dissolved in 1,2-dichloroethane (0.2 ml). To this solution is added valerylchloride (9 mg, 8.95 µl, 0.075 mmol) and the stirring is continued for 2 h. Then 1,2-dichloroethane (0.4 ml) and tris-(2-aminoethyl) amine polystyrene (3.4 mmol/g, 22 mg, 0.075 mmol) are added. After 30 min of shaking the resin is filtered off. Then

methylisocyanate polystyrene (2.5 mmol/g, 30 mg, 0.075 mmol) is added as well as 1,2-dichloroethane (0.5 ml) and the resulting suspension is stirred for 2 h. It is filtered and the organic filtrate is washed with an aqueous KH_2PO_4 solution (pH = 4) and water. Finally the organic phase is dried over Na_2SO_4 and evaporated to dryness yielding the title compound: t_R = 2.62 min (LC-2), ESI-MS (pos.): m/z 510.49 $[M+H]^+$; ^{1}H-NMR (DMSO-d_6 at 100°C): δ (ppm) 0.80 (t, 3H, CH_2CH_3), 1.19 (m, 2H, CH_2CH_3), 1.37 (m, 2H, $CH_2CH_2CH_3$), 1.40 (s, 9H, *t*Bu), 1.91 (m, 2H, CH_2CH_2N), 2.08 (m, 1H, $COCH_a$), 2.24 (m, 1H, $COCH_b$), 2.71-2.83 (m, 2H, CH_2Ph), 3.30 (m, 2H), 3.32-3.43 (m, 4H), 4.98 (m, 2H, CH_2CO_2), 7.12-7.26 (m, 7 H_{arom}), 7.50 (m, 2 H_{arom}).

Alternatively, Precursor Q-01b is synthesized analogous to the procedure described for Precursor K-01b, using alkylating agent Q-01d in place of K-01d.

All the Precursors of the following Table 27 are prepared analogous to the procedures described for Precursor Q-01b.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
L-01b	*tert*-Butyl {2-[3-(pentanoyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C27H35N3O3S 481.66	2.63 (LC-2)	482.45
L-02b	*tert*-Butyl {2-[3-(diphenylacetyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C36H37N3O3S 591.77	2.79 (LC-2)	592.57
L-03b	*tert*-Butyl {2-[3-(phenyl-phenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C30H33N3O3S 515.67	2.59 (LC-2)	516.48
L-04b	*tert*-Butyl (2-{3-[(3,3-diphenyl-propionyl)-phenyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C37H39N3O3S 605.80	2.78 (LC-2)	506.59
L-05b	*tert*-Butyl {2-[3-(benzenesulfonyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C28H31N3O4S2 537.70	2.57 (LC-2)	538.40
L-06b	rac *tert*-Butyl {2-{3-[(2-cyclohexyl-2-phenyl-acetyl)-phenyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C36H43N3O3S 597.82	3.02 (LC-2)	598.62

L-07b	*tert*-Butyl {2-[3-(1,3-diphenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C29H32N4O3S 516.66	2.51 (LC-2)	517.44
L-08b	*tert*-Butyl {2-[3-(3-benzyl-1-phenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C30H34N4O3S 530.69	2.48 (LC-2)	531.46
M-01b	*tert*-Butyl (2-{3-[pentanoyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C32H44N4O3S 564.79	2.66 (LC-2)	565.61
M-02b	*tert*-Butyl (2-{3-[diphenylacetyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C41H46N4O3S 674.91	2.90 (LC-2)	675.67
M-03b	*tert*-Butyl (2-{3-[phenylmethanesulfonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C34H42N4O4S2 634.86	2.54 (LC-2)	635.59
M-04b	*tert*-Butyl (2-{3-[phenylacetyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C35H42N4O3S 598.81	2.64 (LC-2)	599.64
M-05b	*tert*-Butyl (2-{3-[(3,3-diphenyl-propionyl)-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C42H48N4O3S 688.93	2.90 (LC-2)	689.70
M-06b	*tert*-Butyl (2-{3-[1-(4-piperidin-1-yl-phenyl)-3-propyl-ureido]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C31H43N5O3S 565.78	2.30 (LC-2)	566.63
M-07b	*tert*-Butyl (2-{3-[benzenesulfonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C33H40N4O4S2 620.84	2.60 (LC-2)	621.57
N-01b	*tert*-Butyl [2-(3-{[(4-ethyloxycarbonyl)-phenyl]-pentanoyl-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C30H39N3O5S 553.72	2.67 (LC-2)	554.52
N-02b	*tert*-Butyl [2-(3-{diphenylacetyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C39H41N3O5S 663.84	2.83 (LC-2)	664.65
N-03b	*tert*-Butyl (2-{3-[(4-ethyloxycarbonylphenyl)-(phenylacetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C33H37N3O5S 587.74	2.64 (LC-2)	588.56

N-04b	*tert*-Butyl [2-(3-{diphenylpropionyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C40H43N3O5S 677.86	2.83 (LC-2)	678.67
N-05b	rac *tert*-Butyl [2-(3-{(2-cyclohexyl-2-phenyl-acetyl)-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C39H47N3O5S 669.88	3.07 (LC-2)	670.70
O-01b	*tert*-Butyl {2-[3-(benzyl-pentanoyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C28H37N3O3S 495.69	2.59 (LC-2)	496.47
O-02b	*tert*-Butyl {2-[3-(benzyl-diphenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C37H39N3O3S 605.80	2.78 (LC-2)	606.59
O-03b	*tert*-Butyl {2-[3-(benzyl-phenylmethanesulfonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C30H35N3O4S2 565.76	2.61 (LC-2)	566.51
O-04b	*tert*-Butyl {2-[3-(benzyl-phenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C31H35N3O3S 529.70	2.57 (LC-2)	530.50
O-05b	*tert*-Butyl (2-{3-[benzyl-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C38H41N3O3S 619.83	2.76 (LC-2)	620.61
O-06b	*tert*-Butyl {2-[3-(1-benzyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C27H36N4O3S 496.67	2.42 (LC-2)	497.49
O-07b	*tert*-Butyl {2-[3-(benzenesulfonyl-benzyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C29H33N3O4S2 551.73	2.63 (LC-2)	552.49
O-08b	rac *tert*-Butyl(2-{3-[benzyl-(2-cyclohexyl-2-phenyl-acetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C37H45N3O3S 611.85	2.96 (LC-2)	612.64
P-01b	*tert*-Butyl {2-[3-(cyclopropyl-pentanoyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C24H35N3O3S 445.63	2.48 (LC-2)	440.34
P-02b	*tert*-Butyl (2-{3-[(butane-1-sulfonyl)-cyclopropyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C23H35N3O4S2 481.68	2.48 (LC-2)	482.45
P-03b	*tert*-Butyl {2-[3-(cyclopropyl-diphenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C33H37N3O3S 555.74	2.68 (LC-2)	556.56

P-04b	*tert*-Butyl {2-[3-(cyclopropyl-phenylmethanesulfonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C26H33N3O4S2 515.70	2.50 (LC-2)	516.42
P-05b	*tert*-Butyl {2-[3-(cyclopropyl-phenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C27H33N3O3S 479.64	2.45 (LC-2)	480.41
P-06b	*tert*-Butyl (2-{3-[cyclopropyl-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C34H39N3O3S 569.77	2.67 (LC-2)	570.58
P-07b	*tert*-Butyl {2-[3-(1-cyclopropyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C23H34N4O3S 446.61	2.30 (LC-2)	447.47
P-08b	*tert*-Butyl {2-[3-(benzenesulfonyl-cyclopropyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C25H31N3O4S2 501.67	2.50 (LC-2)	502.40
P-09b	rac *tert*-Butyl (2-{3-[(2-cyclohexyl-2-phenyl-acetyl)-cyclopropyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C33H43N3O3S 561.79	2.90 (LC-2)	562.62
Q-02b	*tert*-Butyl (2-{3-[(butane-1-sulfonyl)-phenethyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C28H39N3O4S2 545.77	2.68 (LC-2)	546.49
Q-03b	*tert*-Butyl {2-[3-(diphenylacetyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C38H41N3O3S 619.83	2.79 (LC-2)	620.61
Q-04b	*tert*-Butyl {2-[3-(phenethyl-phenylmethanesulfonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C31H37N3O4S2 579.78	2.66 (LC-2)	580.53
Q-05b	*tert*-Butyl {2-[3-(phenethyl-phenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C32H37N3O3S 543.73	2.62 (LC-2)	544.52
Q-06b	*tert*-Butyl (2-{3-[(3,3-diphenyl-propionyl)-phenethyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C39H43N3O3S 633.85	2.80 (LC-2)	634.63
Q-07b	*tert*-Butyl {2-[3-(1-phenethyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C28H38N4O3S 510.70	2.48 (LC-2)	511.51
Q-08b	*tert*-Butyl {2-[3-(benzenesulfonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C30H35N3O4S2 565.76	2.68 (LC-2)	566.51

R-01b	*tert*-Butyl (2-{3-[(2,2-diphenyl-ethyl)-pentanoyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C35H43N3O3S 585.81	2.78 (LC-2)	586.58
R-02b	*tert*-Butyl (2-{3-[diphenylacetyl-(2,2-diphenyl-ethyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C44H45N3O3S 695.93	2.90 (LC-2)	696.71
R-03b	*tert*-Butyl (2-{3-[(2,2-diphenyl-ethyl)-phenylmethanesulfonyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C37H41N3O4S2 655.88	2.78 (LC-2)	656.62
R-04b	*tert*-Butyl (2-{3-[(2,2-diphenyl-ethyl)-phenylacetyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C38H41N3O3S 619.83	2.75 (LC-2)	620.61
R-05b	*tert*-Butyl (2-{3-[(2,2-diphenyl-ethyl)-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-aceate	C45H47N3O3S 709.95	2.90 (LC-2)	710.73
R-06b	*tert*-Butyl (2-{3-[1-(2,2-diphenyl-ethyl)-3-propyl-ureido]-propylsulfanyl}-benzoimidazol-1-yl)-acetate	C34H42N4O3S 586.80	2.62 (LC-2)	587.60
T-02b	*tert*-Butyl [2-(3-pentanoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C21H31N3O3S 405.56	2.23 (LC-2)	406.44
T-03b	*tert*-Butyl {2-[3-(butane-1-sulfonylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C20H31N3O4S2 441.61	2.32 (LC-2)	442.38
T-04b	*tert*-Butyl [2-(3-diphenylacetylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C30H33N3O3S 515.67	2.50 (LC-2)	516.48
T-05b	*tert*-Butyl [2-(3-phenylmethanesulfonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C23H29N3O4S2 475.63	2.35 (LC-2)	476.40
T-06b	*tert*-Butyl [2-(3-phenylacetylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C24H29N3O3S 439.57	2.24 (LC-2)	440.40
T-07b	*tert*-Butyl {2-[3-(3,3-diphenyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C31H35N3O3S 529.70	2.47 (LC-2)	530.50
T-08b	*tert*-Butyl {2-[3-(3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C20H30N4O3S 406.55	2.08 (LC-2)	407.40

T-09b	*tert*-Butyl [2-(3-benzenesulfonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate	C22H27N3O4S2 461.60	2.33 (LC-2)	462.38
T-10b	rac *tert*-Butyl {2-[3-(2-cyclohexyl-2-phenyl-acetylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C30H39N3O3S 521.72	2.67 (LC-2)	522.53
T-11b	*tert*-Butyl {2-[3-(3-phenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetate	C23H28N4O3S 440.56	2.23 (LC-2)	441.42

Table 27

Alkylating agent N-05d

rac 4-[(3-Chloro-propyl)-(2-cyclohexyl-2-phenyl-acetyl)-amino]-benzoic acid ethyl ester

To a solution of 4-(2-cyclohexyl-2-phenyl-acetylamino)-benzoic acid ethyl ester (Starting material N-05e, 1 g, 2.74 mmol) and 1,3-iodochloropropane (559 mg, 294 µl, 2.74 mmol, 1 eq.) in dry DMF (10 ml) is added sodium hydride (60% w/w in oil, 72 mg, 3 mmol). After addition is complete, the resulting slurry is allowed to stir for 1 h. Then the same quantity of 1,3-iodochloropropane and of sodium hydride are added again and the resulting slurry is heated up to 50°C overnight. After cooling to rt, water is added until pH=7 and the water phase is extracted twice with AcOEt. The organic phase is washed with water / brine (1:1). The organic phase is dried over $MgSO_4$ and the solvent evaporated to afford a yellow oil containing some DMF. It is purified by flash chromatography on silica-gel (AcOEt / heptane / AcOH, 1:9:0.5), yielding the title compound (365 mg) in 30% as a colourless oil: t_R = 8.74 min (LC-1), ESI-MS (pos.): m/z 442.20 $[M+H]^+$.

Starting material N-05e

rac 4-(2-Cyclohexyl-2-phenyl-acetylamino)-benzoic acid ethyl ester

To a flask containing thionyl chloride (1.52 g, 929 µl, 12.8 mmol) and 1 drop of DMF is added cyclohexylphenylacetic acid (1.87 g, 8.54 mmol). The resulting solution is stirred for 1 h. The thionyl chloride is evaporated under reduced pressure and the resulting crude acid chloride is diluted in dichloromethane (15 ml). To this solution is added dropwise a solution of 4-amino-benzoic acid ethyl ester (1.41 g, 8.54 mmol) and

triethylamine (1.49 ml, 1.08 g, 10.67 mmol) in dichloromethane (15 ml). The resulting mixture is stirred for 30 min at rt. It is diluted with dichloromethane and the resulting organic phase is washed with a 10% aqueous citric acid solution, with a saturated aqueous Na_2CO_3 solution and with water. It is dried over Na_2SO_4 and the solvent is evaporated *in vacuo*. The crude residue is purified on silica gel (AcOEt / heptane, 1:4), yielding the title compound (3.04 g) in 97% as a white solid: t_R = 8.00 min (LC-1), ESI-MS (pos.): m/z 366.18 $[M+H]^+$, ESI-MS (neg.): m/z 364.25 $[M-H]^+$.

Alkylating agent Q-01d

Pentanoic acid (3-chloro-propyl)-phenethyl-amide

To a solution of valeryl chloride (342 mg, 338 µl, 2.83 mmol) in dichloromethane (6 ml) and cooled to 0°C is added a solution of (3-chloro-propyl)-phenethyl-amine (Starting material Q-01e, 560 mg, 2.83 mmol). The colourless solution turns yellow and after 2 min, a solid crystallizes out. Upon dropwise addition of Et_3N (315 mg, 409 µl, 2.83 mmol) the solution turns colourless again and the solid dissolves instantaneously. The mixture is allowed to stir for 4 h at which time yet again a solid had crystallized out. Saturated aqueous NH_4Cl solution is added and the organic phase is washed once with some saturated aqueous $NaHCO_3$ solution and dried over Na_2SO_4. The solvent is removed *in vacuo* and the residue is dried under high *vacuum*, yielding the title compound as an orange oil: t_R = 2.48 min (LC-2), ESI-MS (pos.): m/z 282.07 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 0.86-0.97 (m, 3H, CH3), 1.23-1.44 (m, 4H, $C\underline{H_2}CH_3$), 1.55 (quint., 1H, $C\underline{H_2}CH_2CH_3$), 1.65 (quint., 1H, $C\underline{H_2}CH_2CH_3$), 1.95 (quint., 2H, $C\underline{H_2}CH_2N$), 2.03-2.19 (m, 2H, CH2C=O), 2.90 (t, 2H, CH_2Ph), 3.35-3.59 (m, 6H), 7.15-7.34 (m, 2 H_{arom}).

Starting material Q-01e

(3-Chloro-propyl)-phenethyl-amine

This compound is synthesized according to the procedure described in Brinner, K. M.; Kim, J. M.; Habashita, H.; Gluzman, I. Y.; Goldberg, D. E.; Ellman, J. A., Bioorg. Med. Chem. 2002, *10*, 3649, 3661.

A mixture of phenethylamine (7.1 g, 7.38 ml, 58.5 mmol) and bromochloropropane (3.07 g, 1.93 ml, 19.5 mmol) in acetonitrile (15 ml) is stirred for 16 h. In the course of

the reaction a white crystalline solid forms. Saturated aqueous $NaHCO_3$ solution is added to adjust the pH to 9-10. The free amine is extracted three times with AcOEt. The combined organic phases are dried over Na_2SO_4. Evaporation of the solvent *in vacuo* yields a yellow oil. It is purified by chromatography on silica-gel (dichloromethane / MeOH, 95:5), yielding the title compound (1.02 g) in 26% as a slightly yellow oil which crystallizes on standing: ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.91 (quint., 2H, $C\underline{H}_2CH_2N$), 2.75 (m, 4H), 2.81-2.89 (m, 2H), 3.59 (t, 2H, $C\underline{H}_2Cl$), 7.20 (m, 3 H_{arom}), 7.24-7.32 (m, 2 H_{arom}).

Example S-01a

[2-(3-{Butyloxycarbonyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid

tert-Butyl [2-(3-{butyloxycarbonyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate (Precursor S-01b, 233 mg, 0.41 mmol) is dissolved in TFA / dichloromethane (1:1, 5 ml). The solution is allowed to stir at rt overnight. Evaporation of the solvents *in vacuo* and drying under high *vacuum* yields the title compound (206 mg) in 97% as an off-white solid: t_R = 6.71 min (LC-1), ESI-MS (pos.): m/z 514.23 $[M+H]^+$, ESI-MS (neg.): m/z 512.31 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 0.86 (t, 3H, CH_2CH_3), 1.25 (m, 2H, CH_2CH_3), 1.39 (t, 3H, OCH_2CH_3), 1.50 (quint., 2H, OCH_2CH_2), 1.89 (br. t, 2H, SCH_2CH_2), 3.38 (br. t, 2H, SCH_2), 3.81 (m, 2H, CH_2N), 4.04 (t, 2H, OCH_2CH_2), 4.39 (q, 2H, OCH_2CH_3)4.88 (s, 2H, CH_2CO_2), 7.20 (d, 2 H_{arom}), 7.40 (m, 2H_{arom}), 7.59 (br. s, 1H, ac. H), 7.71 (d, 2 H_{arom}), 8.14 (d, 2 H_{arom}).

Precursor S-01b

tert-Butyl [2-(3-{butyloxycarbonyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetate

To a suspension of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate 3-I, 264 mg, 1 mmol) and K_2CO_3 (276 mg, 2 mmol, 2 eq.) in acetone (3 ml) are added 4-[butoxycarbonyl-(3-chloro-propyl)-amino]-benzoic acid ethyl ester (341 mg, 1 mmol) and a few crystals of sodium iodide. The resulting mixture is allowed to stir at reflux for 36 h. It is then cooled down and filtered on a fritted funnel to remove all solid impurities. Evaporation of the solvent *in vacuo* affords a crude oil that is purified by

chromatography on silica gel (AcOEt / heptane, 1:4) yielding the title compound (280 mg) in 49% as a white solid: t_R = 8.07 min (LC-1), ESI-MS (pos.): m/z 570.31 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 0.88 (t, 3H, CH_2CH_3), 1.25-1.32 (m, 2H, CH_2CH_3), 1.34 (t, 3H, OCH_2CH_3), 1.40 (s, 9H, *t*Bu), 1.50 (m, 2H, OCH_2CH_2), 2.05 (quint., 2H, SCH_2CH_2), 3.38 (br. t, 2H, SCH_2), 3.87 (m, 2H, CH_2N), 4.06 (t, 2H, OCH_2CH_2), 4.35 (q, 2H, OCH_2CH_3), 4.66 (s, 2H, CH_2CO_2), 7.14-7.24 (m, 3 H_{arom}), 7.28 (d, 2 H_{arom}), 7.68 (m, 2 H_{arom}), 8.00 (d, 2 H_{arom}).

Alkylating agent S-01d

4-[Butoxycarbonyl-(3-chloro-propyl)-amino]-benzoic acid ethyl ester

is prepared analogous to the procedure described for alkylating agent K-01d, substituting the appropriate carbamate for phenethyl-carbamic acid *tert*-butyl ester. It is obtained as a colourless oil: t_R = 2.60 min (LC-2), MS (pos.): m/z 342.17 $[M+H]^+$.

Example T-01a

[2-(3-*tert*-Butoxycarbonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid

is prepared analogous to the procedure described for Example J-01a, using Precursor T-01b in place of J-01b: t_R = 1.78 min (LC-2), ESI-MS (pos.): m/z 366.31 $[M+H]^+$, ESI-MS (neg.): m/z 364.40 $[M-H]^+$.

Precursor T-01b

tert-Butyl [2-(3-*tert*-butoxycarbonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate

A solution of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 502 mg, 1.9 mmol) and DBU (289 mg, 284 µl, 1.9 mmol) in THF (1 ml) is added onto a solution of (3-bromo-propyl)-carbamic acid *tert*-butyl ester (407 mg, 1.71 mmol) in THF (1 ml). The resulting solution is stirred at rt for 2 h. It becomes slowly turbid and the undesired solid is filtered on a fritted funnel. The solution is diluted with THF (2 ml) and DIPEA (491 mg, 650 µl, 3.8 mmol) is added. The mixture is poured onto a suspension of 2-chlorotrityl chloride resin (200-400 mesh), 1% DVB (1.0 - 1.6 mmol / g, 475 mg, 0.76 mmol) in THF (1 ml) and allowed to stir for 3 h. The resin is filtered and rinsed with THF. The solvent is removed *in vacuo* and the residue diluted with dichloromethane (5 ml). This organic phase is washed with an aqueous citric acid solution (pH=4) and with water. The solvent is evaporated under reduced pressure. The

same purification process is repeated using dichloromethane instead of THF as the solvent. The obtained organic phase is washed with a saturated aqueous KH_2PO_4 solution and water. Evaporation of the solvent *in vacuo* affords a residue that is purified by flash chromatography on silica-gel (AcOEt / heptane, 1:2), yielding the title compound (587 mg) in 73% as a colourless oil: t_R = 2.41 min (LC-2), ESI-MS (pos.): m/z 422.50 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.37 (s, 9H, *tBu*), 1.39 (s, 9H, *tBu*), 1.74 (quint. 2H, CH_2CH_2N), 3.20 (dd, 2H), 3.38 (t, 2H), 4.67 (s, 2H, CH_2CO_2), 5.82 (br. s, 1H, NH), 7.10-7.29 (m, $3H_{arom}$), 7.65 (m, $1H_{arom}$).

Precursor T-12b

tert-Butyl [2-(3-benzoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetate

To a suspension of 3-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl-ammonium chloride (Precursor U-08b, 6 mg, 0.02 mmol) in dichloromethane (0.4 ml) are added subsequently DIPEA (10mg, 15 µl, 0.085 mmol) and benzoyl chloride (3.9 mg, 3.24 µl, 0.03 mmol) and the resulting solution is allowed to stir for 1 h at rt. Tris-(2-aminoethyl) amine polystyrene (3.4 mmol/g, 33mg, 0.11 mmol) is added and the mixture is allowed to stir for another 3 h at rt. The solvent is evaporated and the residue dried under high *vacuum*, yielding the title compound as a colourless oil: t_R = 2.62 min (LC-2), ESI-MS (pos.): m/z 510.49 $[M+H]^+$.

Precursors T-13b to T-27b of the following Table 28 are prepared using a procedure analogous to that described for Precursor T-12b, substituting the appropriate acyl chloride for benzoyl chloride.

Ex.	Name	Formula weight	Mol	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^-$
T-13b	{2-[3-(Cyclohexanecarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid tert-butyl ester	C23H33N3O3S 431.59		2.34 (LC-2)	432.29	n/a
T-14b	{2-[3-(4-Methoxy-benzoylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid tert-butyl ester	C24H29N3O4S 455.57		na (LC-2)	n/a	n/a

T-15b	(2-{3-[(Furan-2-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid tert-butyl ester	C21H25N3O4S 415.51	2.15 (LC-2)	416.41	n/a
T-16b	{2-[3-(Cyclopropanecarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid tert-butyl ester	C20H27N3O3S 389.51	2.10 (LC-2)	390.43	388.47
T-17b	(2-{3-[(Naphthalene-1-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid tert-butyl ester	C27H29N3O3S 475.61	2.41 (LC-2)	476.48	474.62
T-18b	{2-[3-(3-Cyclopentyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid tert-butyl ester	C24H35N3O3S 445.63	2.45 (LC-2)	446.44	444.58
T-19b	{2-[3-(2,2-Dimethyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid tert-butyl ester	C21H31N3O3S 405.56	2.26 (LC-2)	406.47	n/a
T-20b	{2-[3-(3-Phenyl-acryloylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid tert-butyl ester	C25H29N3O3S 451.59	2.33 (LC-2)	452.48	450.49
T-21b	{2-[3-(3-Phenyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid tert-butyl ester	C25H31N3O3S 453.60	2.29 (LC-2)	454.47	452.60
T-22b	N-[3-(1-tert-Butoxycarbonylmethyl-1H-benzoimidazol-2-ylsulfanyl)-propyl]-oxalamic acid ethyl ester	C20H27N3O5S 421.52	2.39 (LC-2)	422.45	420.52
T-23b	(2-{3-[(Biphenyl-4-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid tert-butyl ester	C29H31N3O3S 501.65	2.55 (LC-2)	502.47	500.48
T-24b	(2-{3-[(Pyridine-3-carbonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid tert-butyl ester	C22H26N4O3S 426.54	1.97 (LC-2)	427.39	425.53
T-25b	{2-[3-(3,3-Dimethyl-butyrylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid tert-butyl ester	C22H33N3O3S 419.59	2.30 (LC-2)	420.46	n/a
T-26b	[2-(3-Octanoylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid tert-butyl ester	C24H37N3O3S 447.64	2.54 (LC-2)	448.50	446.57

T-27b	{2-[3-(4-Bromo-benzoylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid tert-butyl ester	C23H26BrN3O3S 504.45	2.45 (LC-2)	506.38	504.46

Table 28

Example U-01a

[2-(3-Phenethylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid

tert-Butyl {2-[3-(*tert*-butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate (Precursor J-01b, 5.5 mg, 0.015 mmol) is dissolved in TFA / dichloromethane (1:1, 1.5 ml) and stirred at rt for 1.5 h. The solvents are evaporated under reduced pressure and the residue is dried under high *vacuum,* yielding the pure title compound: t_R = 1.51 min (LC-2), ESI-MS (pos.): m/z 370.39 $[M+H]^+$; ESI-MS (neg.): m/z 368.42 $[M-H]^+$.

Examples U-02a to U-07a of the following Table 29 are prepared analogous to the procedure described for Example U-01a, using Precursors J-02b to J-07b in place of J-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
U-02a	{2-[3-(4-Piperidin-1-yl-phenylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C23H28N4O2S 424.567	1.41 (LC-2)	425.43	n/a
U-04a	[2-(3-Benzylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C19H21N3O2S 355.461	1.45 (LC-2)	356.38	354.47
U-06a	[2-(3-Phenylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C18H19N3O2S 341.434	1.65 (LC-2)	342.30	340.39
U-07a	{2-[3-(2,2-Diphenyl-ethylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C26H27N3O2S 445.585	1.73 (LC-2)	446.39	n/a

Table 29

Precursor U-01b

[3-(1-*tert*-Butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-phenethyl-ammonium chloride

tert-Butyl {2-[3-(*tert*-butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetate (Precursor J-01b, 199 mg, 0.38 mmol) is dissolved in a 1M HCl solution in ethyl acetate (1.89 ml). The resulting solution is stirred at rt for 1 h. The solvent is evaporated and the crude solid is dissolved in dichloromethane, the resulting organic phase is washed with a saturated aqueous $NaHCO_3$ solution and with water. Evaporation of the solvent *in vacuo* and chromatography of the residue on silica-gel (dichloromethane / MeOH, 92:8) yields the title compound (107 mg) in 61% as a white solid: t_R = 2.62 min (LC-2), ESI-MS (pos.): m/z 510.49 $[M+H]^+$.

Precursors U-02b to U-08b of the following Table 30 are prepared analogous to the procedure described for Precursor U-01b, using Precursors J-02b to J-08b in place of J-01b.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
U-02b	[3-(1-*tert*-Butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-(4-piperidin-1-yl-phenyl)-ammonium chloride	C27H37ClN4O2S 517.12	1.82 (LC-2)	481.43
U-03b	[3-(1-*tert*-Butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-(4-ethoxycarbonyl-phenyl)-ammonium chloride	C25H32ClN3O4S 506.05	2.55 (LC-2)	470.41
U-04b	Benzyl-[3-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-ammonium chloride	C23H30ClN3O2S 448.02	1.81 (LC-2)	411.55
U-05b	[3-(1-*tert*-Butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-cyclopropyl-ammonium chloride	C19H28ClN3O2S 397.96	1.70 (LC-2)	362.36

U-06b	[3-(1-*tert*-Butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-phenyl-ammonium chloride	C22H28ClN3O2S 433.99	2.39 (LC-2)	398.4
U-07b	[3-(1-*tert*-Butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl]-(2,2-diphenyl-ethyl)-ammonium chloride	C30H36ClN3O2S 538.14	1.97 (LC-2)	502.46
U-08b	3-(1-*tert*-Butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-propyl-ammonium chloride	C16H24ClN3O2S 357.90	1.60 (LC-2)	322.37

Table 30

Example V-01a

{2-[2-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid

is prepared analogous to the procedure described for Example G-01a, using Precursor V-01b in place of G-01b: t_R = 5.21 min (LC-1), ESI-MS (pos.): m/z 382.15 $[M+H]^+$, ESI-MS (neg.): m/z 380.20 $[M-H]^+$.

Example V-02a

[2-(2-*tert*-Butoxycarbonylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid

tert-Butyl [2-(2-*tert*-butoxycarbonylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetate (Precursor V-02b, 28.5 mg, 0.07 mmol) is suspended in 0.2 M aqueous NaOH (2.1 ml), THF (3.95 ml) is then added and the initially turbid suspension becomes a clear solution. After 7 h, 1M aqueous HCl solution (420 µl) is added. The solution is diluted with water (10 ml) and extracted with dichloromethane (15 ml). The organic phase is dried over $MgSO_4$ filtered over a fritted funnel and the solvents are evaporated *in vacuo*. Drying of the residue under high *vacuum* yields the title compound (19 mg) in 77% as a colourless solid: t_R = 1.74 min (LC-2), ESI-MS (pos.): m/z 352.17 $[M+H]^+$, ESI-MS (neg.): m/z 350.20 $[M-H]^+$.

Examples V-03a to V-05a of the following Table 31 are prepared analogous to the procedure described for Example V-02a, using Precursors V-03b to V-05b in place of V-02b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
V-03a	[2-(2-Butoxycarbonylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C16H21N3O4S 351.42	1.74 (LC-2)	352.2	350.2
V-04a	[2-(2-Diphenylacetylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C25H23N3O3S 445.53	2.00 (LC-2)	446.26	444.29
V-05a	{2-[2-(3-Phenyl-ureido)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C18H18N4O3S 370.43	1.58 (LC-2)	371.22	369.12

Table 31

Precursor V-01b

tert-Butyl {2-[2-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate

is prepared using a procedure analogous to that described for Precursor G-01b, substituting 2-(2-bromo-ethyl)-isoindole-1,3-dione for G-01d: t_R = 6.84 min (LC-1), ESI-MS (pos.): m/z 438.35 $[M+H]^+$.

Precursor V-02b

tert-Butyl [2-(2-*tert*-butoxycarbonylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetate

To a solution of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 1.31 g, 4.97 mmol) in dry THF (2.6 ml) cooled to 0°C is added a solution of DBU (756.6 mg, 742.5 µl, 0.47 mmol) in dry THF (1 ml). This yields a paste that is diluted with dry THF (2.5 ml). A solution of (2-bromo-ethyl)-carbamic acid *tert*-butyl ester (1.17 g, 5.22 mmol) in dry THF (2.6 ml) is then added and the resulting mixture is allowed to stir for 2 h. The solvent is removed under reduced pressure and saturated aqueous KH_2PO_4 solution (50 ml) is added. The product is extracted with AcOEt (150 ml), the organic phase is washed once with water and once with brine and dried over Na_2SO_4. The solvent is removed *in vacuo* and the crude mixture is purified by flash chromatography on silica-gel (AcOEt / heptane, 1:12), yielding the title compound

(1.41 g) in 69% as a colourless oil: t_R = 2.35 min (LC-2), ESI-MS (pos.): m/z 408.27 $[M+H]^+$.

Precursor V-03b

tert-Butyl [2-(2-butoxycarbonylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetate

tert-butyl [2-(2-*tert*-butoxycarbonylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetate (Precursor V-02b) is dissolved in 3M HCl in AcOEt and stirred for 1 h at rt. Evaporation of the solvent *in vacuo* yields 2-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-ethyl-ammonium chloride as a colourless solid. To a solution of *n*-butylchloroformate (14.9 mg, 14 µl, 0.11 mmol) in dry THF (0.5 ml) cooled to 0°C is added a solution of HOBt (17.3 mg, 0.11 mmol) and DIPEA (18 mg, 23.8 µl, 0.14 mmol) in dry THF (0.5 ml). The resulting mixture is stirred for 10 min. It is then added dropwise at 0°C onto a solution of 2-(1-*tert*-butoxycarbonylmethyl-1*H*-benzoimidazol-2-ylsulfanyl)-ethyl-ammonium chloride (30 mg, 0.09 mmol) and DIPEA (11.2 mg, 14.9 µl, 0.09 mmol) in dry THF (0.7 ml). The resulting mixture is stirred for 1 h at rt. Then tris-(2-aminoethyl) amine polystyrene (3.4 mmol/g, 25.6 mg) is added and the resulting slurry is allowed to stir for 2 h at rt and then filtered. The solvent is removed *in vacuo* and the residue is diluted with dichloromethane (5 ml). This organic phase is washed once with a saturated aqueous $NaHCO_3$ solution and a saturated aqueous KH_2PO_4 solution. Evaporation of the solvent *in vacuo* yields the title compound (17.1 mg) in 48% as a colourless oil: t_R = 2.35 min (LC-2), ESI-MS (pos.): m/z 408.29 $[M+H]^+$.

Precursors V-04b and V-05b of the following Table 32 are prepared using a procedure analogous to that described for Precursor V-03b, substituting the appropriate acid chloride or isocyanate for *n*-butylchloroformate. In the case of the isocyanate, no HOBt is used.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
V-04b	*tert*-Butyl [2-(2-diphenylacetylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetate	C29H31N3O3S 501.64	2.46 (LC-2)	502.33	500.3

V-05b	*tert*-Butyl {2-[2-(3-phenyl-ureido)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate	C22H26N4O3S 426.53	2.17 (LC-2)	427.28	425.3

Table 32

Intermediate **4-I**

tert-Butyl [2-(2-bromo-ethylsulfanyl)-benzoimidazol-1-yl]-acetate

To a solution of *tert*-butyl (2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate **3-I**, 0.5 g, 1.9 mmol) in THF (1 ml) is added DBU (304 mg, 300 µl, 2 mmol) and the resulting mixture is allowed to stir 2 min at rt. This solution is added slowly dropwise onto dibromoethane (7.5 ml, 88 mmol). The resulting solution is allowed to stir at rt for 1 h. After addition of dichloromethane (20 ml) the organic phase is washed with aqueous citric acid solution (pH=4), with water and with brine. Evaporation of the solvents *in vacuo* yields the title compound as a colourless oil: t_R = 1.43 min (LC-2), ESI-MS (pos.): m/z 373.23 $[M+H]^+$.

Example W-01a

[2-(2-Phenylamino-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid

To *tert*-butyl [2-(2-bromo-ethylsulfanyl)-benzoimidazol-1-yl]-acetate (Intermediate **4-I**, 25 mg, 0.065 mmol) in EtOH (0.7 ml) is added aniline (31.3 mg, 0.34 mmol). The resulting mixture is heated up to 70°C for 1 h. After cooling the solvent is evaporated *in vacuo* and the crude ester is dissolved in TFA / dichloromethane (3:2, 2 ml) and stirred at rt for 2 h. Evaporation of the solvents *in vacuo* affords a crude product that is purified by chromatography on silica-gel (dichlromethane / MeOH, 100:7.5), yielding the pure title compound: t_R = 2.11 min (LC-2), ESI-MS (pos.): m/z 328.33 $[M+H]^+$, ESI-MS (neg.): m/z 326.34 $[M-H]^+$.

Example (5/6)-Me-D-01a

{2-[2-(4-Chloro-phenoxy)-ethylsulfanyl]-5-methyl-benzoimidazol-1-yl}-acetic acid and its 6-methyl regioisomer

A solution of *tert*-butyl-{2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-5-methyl-benzoimidazol-1-yl}-acetate and its 6-methyl regioisomer (Precursor (5/6)-Me-D-01b, 80.5 mg, 0.15 mmol) in TFA / dichloromethane (1:1, 0.5 ml) is stirred overnight at rt.

The solvents are evaporated *in vacuo*. The product solidifies by addition of AcOEt / heptane (1:1, 1 ml) and sonication. It is filtered and rinsed with the same solvent twice then dried under high *vacuum*. The title compound and its 6-methyl regioisomer (42 mg) are obtained as a (3:2) mixture in 74% total yield as a white solid: t_R = 6.32 min (LC-1), ESI-MS (pos.): m/z 377.18 $[M+H]^+$, ESI-MS (neg.): m/z 375.24 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 2.41 (s, 3H, Me), 3.67 (t, 2H, SCH_2), 4.30 (t, 2H, $C\underline{H}_2O$), 4.96 and 4.97 (s, 2H, $C\underline{H}_2CO_2$), 6.97-7.01 (m, 3 H_{arom}), 7.27-7.36 (m, 3 H_{arom}), 7.44 (d, 1 H_{arom}).

Example (5/6)-CN-H-01a

[5-Cyano-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-cyano regioisomer

A solution *tert*-butyl [(5-cyano-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetate and its 6-cyano regioisomer (Precursor (5/6)-CN-H-01b, 20 mg, 0.045 mmol) in TFA / dichloromethane (1:1, 1 ml) is stirred at rt overnight. The solvents are evaporated *in vacuo*. The residue is precipitated in AcOEt / heptane (1:1, containing 1% of AcOH), filtered and dried under high *vacuum*. The title compound and its 6-cyano regioisomer are obtained (5 mg) as a (1:1) mixture in 28% total yield as a white solid: t_R = 5.97 min (LC-1), ESI-MS (pos.): m/z 382.13 $[M+H]^+$, ESI-MS (neg.): m/z 380.14 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 3.82 (s, 3H, Me), 4.72 and 4.73 (s, 2H, SCH_2), 5.03 and 5.04 (s, 2H, CH_2CO_2), 7.44 (t, 1 H_{arom}), 7.58 (dt, 1 H_{arom}), 7.69-7.76 (m, 2H_{arom}), 7.83 (d, 1 H_{arom}), 8.08 and 8.17 (s, 1 H_{arom}), 8.08 (m, 1 H_{arom}).

Example (5/6)-F-E-03a

[2-(4-Ethyloxycarbonyl-butylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid and its 6-fluoro regioisomer

A solution of *tert*-butyl [2-(4-ethyloxycarbonyl-butylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate and its 6-fluoro regioisomer (Precursor (5/6)-F-E-03b, 24 mg, 0.075 mmol) in TFA /dichloromethane (1:1, 2 ml) is stirred overnight at rt. The solvents are evaporated *in vacuo* and the crude mixture is taken up in Et_2O (1 ml) and sonicated. The solid is filtered, rinsed twice with Et_2O and dried under high *vacuum*. The title compound and its 6-fluoro regioisomer are obtained (8 mg) as a (1:1) mixture in 30%

total yield as a white solid: t_R = 1.96 min (LC-2), ESI-MS (pos.): m/z 355.04 $[M+H]^+$, ESI-MS (neg.): m/z 353.13 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.19 (t, 3H, CH_3), 1.72 (m, 4H), 2.36 (t, 2H, CH_2CO), 3.32 (t, 2H, SCH_2), 4.06 (q, 2H, $C\underline{H}_2O$), 5.00 and 5.02(s, 1H, CH2CO2), 7.01 (dt, 1 H_{arom}), 7.39 and 7.47 (dd, 1 H_{arom}), 7.52 (m, 1 H_{arom}).

Examples 6-I-D-02a to (5/6)-F-H-01a of the following Table 33 are prepared using a procedure analogous to one of those described for Examples (5/6)-Me-D-01a, (5/6)-CN-H-01a, or (5/6)-F-E-03a, using Precursors 6-I-D-02b to (5/6)-F-H-01b in place of (5/6)-Me-D-01b, (5/6)-CN-H-01b, or (5/6)-F-E-03b, respectively.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
6-I-D-02a	[6-Iodo-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C17H15IN2O3S 454.283	6.75 (LC-1)	455.18	453.29
(5/6)-Cl-D-01a	{5-Chloro-2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid and its 6-chloro regioisomer	C17H14Cl2N2O3S 397.281	6.98 (LC-1)	397.13	395.18
(4/7)-Me-D-01a	{2-[2-(4-Chloro-phenoxy)-ethylsulfanyl]-4-methyl-benzoimidazol-1-yl}-acetic acid and its 7-methyl regioisomer	C18H17ClN2O3S 376.863	6.49 (LC-1)	377.19	375.24
(5/6)-CN-D-02a	[5-Cyano-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-cyano regioisomer	C18H15N3O3S 353.401	6.18 (LC-1)	354.14	352.14
(5/6)-CN-E-03a	[5-Cyano-2-(4-ethyloxycarbonyl-butylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-cyano regioisomer	C16H17N3O4S 347.394	5.77 (LC-1)	362.16	360.18
(5/6)-CF3-E-03a	[2-(4-Ethyloxycarbonyl-butylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetic acid and its 6-trifluoromethyl regioisomer	C17H19F3N2O4S 404.408	6.46 (LC-1)	405.27	403.36

(5/6)-CF3-H-01a	[2-(3-Methoxycarbonyl-benzylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetic acid and its 6-trifluoromethyl regioisomer	C19H15N2O4F3S 424.398	6.58 (LC-1)	425.16	423.08
(5/6)-F-D-02a	[5-Fluoro-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-fluoro regioisomer	C17H15N2O3FS 346.381	2.1 (LC-2)	345.1	347.08
(5/6)-F-H-01a	[5-Fluoro-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-fluoro regioisomer	C18H15N2O4FS 374.391	2.02 (LC-2)	373.13	375.1

Table 33

Precursor (5/6)-Me-D-01b

tert-Butyl-{2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-5-methyl-benzoimidazol-1-yl}-acetate and its 6-methyl regioisomer

A suspension of 2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-5-methyl-benzoimidazole (Intermediate 5-Me-D-01c, 106 mg, 0.3 mmol), *tert*-butyl bromoacetate (59 mg, 44.3 µl, 0.3 mmol) and K_2CO_3 (83 mg, 0.6 mmol) in DMF (2 ml) is stirred at rt for 3 h. After addition of water, the aqueous phase is extracted twice with AcOEt. The combined organic phases are washed with water / brine (1:1) and dried over Na_2SO_4. Evaporation of the solvent *in vacuo* and drying of the residue under high *vacuum* affords the title compound and its 6-methyl regioisomer (131 mg) as a (3:2) mixture in a quantitative total yield as a colourless oil. It is used without purification in the next step: t_R = 2.73 min (LC-2), ESI-MS (pos.): m/z 433.29 $[M+H]^+$.

Precursor (5/6)-CN-H-01b

tert-Butyl [5-cyano-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetate and its 6-cyano regioisomer

A suspension of 5-cyano-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazole (Intermediate 5-CN-H-01c, 25 mg, 0.075 mmol), *tert*-butyl bromoacetate (12 mg, 9 µl, 0.06 mmol) and K_2CO_3 (30 mg, 0.155 mmol) in acetone (0.3 ml) is stirred at reflux for 2 h. The crude suspension is cooled down and filtered on a short pad of silica gel using

AcOEt as eluent. The solvent is evaporated *in vacuo* and the residue dried under high *vacuum*. The title compound and its 6-cyano regioisomer are obtained as a (1:1) mixture as a brownish oil which is used without purification in the next step: t_R = 2.47 min (LC-2), ESI-MS (pos.): m/z 438.14.29 $[M+H]^+$.

Precursor (5/6)-F-E-03b

tert-Butyl [2-(4-ethyloxycarbonyl-butylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate and its 6-fluoro regioisomer

A suspension of 2-(4-ethyloxycarbonyl-butylsulfanyl)-5-fluoro-benzoimidazole (Intermediate 5-F-E-03c, 44 mg, 0.15 mmol), *tert*-butyl bromoacetate (31 mg, 24 µl, 0.155 mmol) and K_2CO_3 (41 mg, 0.3 mmol) in acetone (0.5 ml) is stirred at reflux for 3 h. The crude suspension is cooled down and filtered on a short pad of silica gel using AcOEt as eluent. The solvent is removed under *vacuum* and the residue purified by flash chromatography on silica-gel (AcOEt / heptane, 3:7). The title compound and its 6-fluoro regioisomer are obtained as a (1:1) mixture as a colourless solid: t_R = 7.25 min (LC-1), ESI-MS (pos.): m/z 411.26 $[M+H]^+$, ESI-MS (neg.): m/z 408.93 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.25 (t, 3H, CH_3), 1.42 and 1.44 (s, 9H, *t*Bu), 1.79 (m, 4H), 2.34 (t, 2H, CH_2CO), 3.36 (dd, 2H, SCH_2), 4.12 (q, 2H, $C\underline{H_2}O$), 4.70 and 4.72 (s, 1H, CH_2CO_2), 6.86 and 7.01 (dd, 1 H_{arom}), 6.94 (t, 1 H_{arom}), 7.39 and 7.56(dd, 1H_{arom}).

Precursors 5-Cl-D-01b to 5-F-H-01b of the following Table 34 as well as Precursor D-01b are prepared using a procedure analogous to one of those described for Precursors (5/6)-Me-D-01b, (5/6)-CN-H-01b or (5/6)-F-E-03b, using Intermediates 5-Cl-D-01c to 5-F-H-01b and D-01c in place of 5-Me-D-01c, 5-CN-H-01c or 5-F-E-03c.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
(5/6)-Cl-D-01b	*tert*-Butyl {5-chloro-2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetate and its 6-chloro regioisomer	C21H22Cl2N2O3S 453.38	2.81 (LC-2)	453.18

(4/7)-Me-D-01b	*tert*-Butyl {2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-4-methyl-benzoimidazol-1-yl}-acetate and its 7-methyl regioisomer	C22H25ClN2O3S 432.96	2.8 (LC-2)	433.23
(5/6)-CN-D-02b	*tert*-Butyl [5-cyano-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetate and its 6-cyano regioisomer	C22H23N3O3S 409.5	2.58 (LC-2)	410.14
(5/6)-CN-E-03b	*tert*-Butyl [5-cyano-2-(4-ethyloxycarbonyl-butylsulfanyl)-benzoimidazol-1-yl]-acetate and its 6-cyano regioisomer	C21H27N3O4S 417.52	2.45 (LC-2)	418.23
(5/6)-CF3-E-03b	*tert*-Butyl [2-(4-ethyloxycarbonyl-butylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetate and its 6-trifluoromethyl regioisomer	C21H27F3N2O4S 460.51	2.64 (LC-2)	461.40
(5/6)-CF3-H-01b	*tert*-Butyl [2-(3-methoxycarbonyl-benzylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetate its 6-trifluoromethyl regioisomer	C23H23F3N2O4S 480.5	7.85 (LC-1)	481.24
(5/6)-F-D-02b	*tert*-Butyl [2-(2-phenoxy-ethylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate and its 6-fluoro regioisomer	C21H23N2O3FS 402.49	2.6 (LC-2)	403.20
(5/6)-F-H-01b	*tert*-Butyl [5-fluoro-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetate its 6-fluoro regioisomer	C22H23N2O4FS 430.50	2.49 (LC-2)	431.16

Table 34

Intermediate D-01c

2-[2-(4-Chloro-phenoxy)-ethylsulfanyl]-benzoimidazole

According to a procedure described by Matthews, C. J.; Clegg, W.; Elsegood, M. R. J.; Leese, T. A.; Thorp, D.; Thornton, P.; Lockart, J. C., J. Chem. Soc. Dalton Trans., 1996, 1531-1538.

A solution of 2-sulfanylbenzimidazole (159 mg, 1.06 mmol) and DIPEA (150 mg, 200 µl, 1.16 mmol) in dry THF (3 ml) is refluxed for half an hour. After cooling to rt, 1-(2-bromo-ethoxy)-4-chloro-benzene (250 mg, 1.06 mmol) is added. After a further 4 h of reflux, the solvents are removed *in vacuo* and the residue purified by flash chromatography on silica gel (AcOEt / heptane, 1:9 to 3:7), yielding the title compound (285 mg) in 88% as a white solid: t_R = 5.40 min (LC-1), ESI-MS (neg.): m/z 303.0 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ 3.76 (t, 2H, SCH_2), 4.31 (t, 2H, OCH_2), 6.76 (d, 2 H_{arom}), 7.18 (d, 2 H_{arom}), 7.22-7.32 (m, 3 H_{arom}), 7.57 (m, 1 H_{arom}).

Intermediate 5-Me-H-01c

2-[2-(4-Chloro-phenoxy)-ethylsulfanyl]-5-methyl-benzoimidazole

A suspension of 5-methyl-1*H*-benzoimidazole-2-thiol (492 mg, 3 mmol), 1-(2-bromo-ethoxy)-4-chloro-benzene (777 mg, 3.3 mmol) and K_2CO_3 (828 mg, 6 mmol) in acetone (10 ml) is refluxed for 3 h. It is cooled down and filtered on filter paper. The solvent is removed *in vacuo* and the crude purified by flash chromatography on silica-gel (AcOEt / heptane, 3:7), yielding the title compound (530 mg) in 55% as an off-white solid: t_R = 2.02 min (LC-2), ESI-MS (pos.): m/z 319.21 $[M+H]^+$, ESI-MS (neg.): m/z 317.23 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.36 (s, 3H, Me), 3.59 (t, 2H, SCH_2), 4.23 (t, 2H, CH_2O), 6.75 (d, 2H_{arom}), 6.97 (d, 1 H_{arom}), 7.13 (d, 2 H_{arom}), 7.18 (s, 1 H_{arom}), 7.34 (d, 1H_{arom}).

Intermediate 5-CN-H-01c

5-Cyano-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazole

A suspension of 5-cyano-1*H*-benzoimidazole-2-thiol (35 mg, 0.2 mmol), 3-bromomethyl-benzoic acid methyl ester (46 mg, 0.2 mmol) and K_2CO_3 (55 mg, 0.4 mmol) in acetone (0.6 ml) and 3 drops of DMF is refluxed for 2 h. It is cooled down and filtered over a short plug of silica gel and rinsed with AcOEt. The solvent is removed under a stream of air. The crude residue is purified by flash chromatography on silica-gel (AcOEt / heptane, 1:2), yielding the title compound (38 mg) in 59% as a yellowish gum: t_R = 6.14 min (LC-1), ESI-MS (pos.): m/z 324.14 $[M+H]^+$, ESI-MS (neg.): m/z 322.22 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 3.92 (s, 3H, Me), 4.67 (s, 2H, SCH_2), 5.29 (s, 1H, NH), 7.36-7.56 (m, 4H_{arom}), 7.65 (d, 1H_{arom}), 7.94 (d, 1H_{arom}), 8.10 (s, 1H_{arom})

Intermediate 5-F-E-03c

2-(4-Ethyloxycarbonyl-butylsulfanyl)-5-fluoro-benzoimidazole

A suspension of 5-fluoro-1*H*-benzoimidazole-2-thiol (168 mg, 1 mmol), 5-bromo-pentanoic acid ethyl ester (188 mg, 0.9 mmol, 145 µl) and K_2CO_3 (276 mg, 2 mmol) in acetone (2 ml) is refluxed for 3 h. It is cooled down and filtered over a short plug of silica gel and rinsed with AcOEt. The solvent is removed *in vacuo*. The crude is purified by flash chromatography on silica-gel (AcOEt / heptane, 1:2), yielding the title compound (190 mg) in 64% as a brown oil: t_R = 1.87 min (LC-2), ESI-MS (pos.): m/z 297.28 $[M+H]^+$, ESI-MS (neg.): m/z 295.30 $[M-H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.25 (t, 3H, CH_3), 1.79 (br. t, 4H), 2.36 (br. t, 2H, CH_2CO), 3.28 (br. t, 2H, SCH_2), 4.14 (q, 2H, $C\underline{H}_2O$), 6.93 (dt, $1H_{arom}$), 7.20 (dd, $1H_{arom}$), 7.41 (dd, $1H_{arom}$).

Intermediates 5-Cl-D-01c to 5-F-H-01c of the following Table 35 are prepared using a procedure analogous to one of those described for Intermediates 5-Me-D-01c, 5-CN-H-01c or 5-F-E-03c, using the appropriate 5-substituted benzimidazole-2-thiol in place of 5-methyl-1*H*-benzoimidazole-2-thiol, 5-cyano-1*H*-benzoimidazole-2-thiol or 5-fluoro-1*H*-benzoimidazole-2-thiol.

Intermediate	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
5-Cl-D-01c	5-Chloro-2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazole	C15H12Cl2N2OS 339.24	7.23 (LC-1)	353.12	355.15
4-Me-D-01c	2-[2-(4-Chloro-phenoxy)-ethylsulfanyl]-4-methyl-benzoimidazole	C16H15ClN2OS 318.82	6.18 (LC-1)	317.13	319.19
5-CN-D-02c	5-Cyano-2-(2-phenoxy-ethylsulfanyl)-benzoimidazole	C16H13N3OS 295.36	6.37 (LC-1)	296.02	294.21
5-CN-E-03c	5-Cyano-2-(4-ethyloxycarbonyl-butylsulfanyl)-benzoimidazole	C15H17N3O2S 303.38	5.96 (LC-1)	304.17	302.22

5-CF3-E-03c	2-(4-Ethyloxycarbonyl-butylsulfanyl)-5-trifluoromethyl-benzoimidazole	C15H17F3N2O2S 346.37	6.66 (LC-1)	347.3	345.4
5-CF3-H-01c	2-(3-Methoxycarbonyl-benzylsulfanyl)-5-trifluoromethyl-benzoimidazole	C17H13F3N2O2S 366.36	4.14 (LC-1)	300.19	298.17
5-F-D-02c	5-Fluoro-2-(2-phenoxy-ethylsulfanyl)-benzoimidazole	C15H13N2OFS 288.345	2.11 (LC-2)	289.19	287.22
5-F-H-01c	5-Fluoro-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazole	C16H13N2O2FS 316.355	6.05 (LC-1)	317.11	315.26

Table 35

Example 5-NO2-C-02a

(2-Benzylsulfanyl-5-nitro-benzoimidazol-1-yl)-acetic acid

tert-Butyl (2-benzylsulfanyl-5-nitro-benzoimidazol-1-yl)-acetate (Precursor 5-NO2-C-02b, 20 mg, 0.05 mmol) is dissolved in TFA / dichloromethane (1:1, 0.5 ml) and stirred for 2 h at rt. The solvents are evaporated under a stream of air and Et_2O (1 ml) is added to the crude mixture. The solid obtained is filtered, rinsed twice with Et_2O and dried under high *vacuum* yielding the title compound (10.4 mg) in 60% as a slightly yellow solid: t_R = 6.30 min (LC-1), ESI-MS (pos.): m/z 344.23 $[M+H]^+$, ESI-MS (neg.): m/z 342.34 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 4.66 (s, 2H, SCH_2), 5.07 (s, 2H, CH_2CO_2), 7.23-7.33 (m, 3 H_{arom}), 7.46 (dd, 2 H_{arom}), 7.74 (d, 1 H_{arom}), 8.13 (dd, 1 H_{arom}), 8.44 (d, 1 H_{arom}).

Examples 5-NO2-D-01a to 6-NO2-G-06a of the following Table 36 are prepared analogous to the procedure described for Example 5-NO2-C-02a, using Precursors 5-NO2-D-01b to 6-NO2-G-06b in place of 5-NO2-C-02b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z [M-H]+

5-NO2-D-01a	{5-Nitro-2-[2-(4-chloro)-phenoxy-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C17H14ClN3O5S 407.833	6.84 (LC-1)	408.12	406.21
(5/6)-NO2-D-02a	5-Nitro-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-Nitro regioisomer	C17H15N3O5S 373.388	6.46 (LC-1)	374.25	372.36
5-NO2-C-02a	(2-Benzylsulfanyl-5-nitro-benzoimidazol-1-yl)-acetic acid	C16H13N3O4S 343.362	6.3 (LC-1)	344.23	342.34
5-NO2-C-05a	[2-(3,3-Diphenyl-propylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid	C24H21N3O4S 447.514	7.24 (LC-1)	448.36	446.4
5-NO2-E-03a	[2-(4-Ethyloxycarbonyl-butylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid	C16H19N3O6S 381.408	6.11 (LC-1)	382.3	380.34
5-NO2-G-06a	{2-[3-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-5-nitro-benzoimidazol-1-yl}-acetic acid	C20H16N4O6S 440.435	6.14 (LC-1)	441.29	439.33
5-NO2-H-01a	[2-(3-Methoxycarbonyl-benzylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid	C18H15N3O6S 401.398	6.24 (LC-1)	402.24	400.28
5-NO2-K-01a	{2-[3-(Butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-5-nitro-benzoimidazol-1-yl}-acetic acid	C25H30N4O6S 514.601	7.37 (LC-1)	513.3	515.2
5-NO2-T-04a	[2-(3-Diphenylacetylamino-propylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid	C26H24N4O5S 504.56	2.24 (c)	505.58	503.54
6-NO2-C-02a	(2-Benzylsulfanyl-6-nitro-benzoimidazol-1-yl)-acetic acid	C16H13N3O4S 343.362	6.27 (LC-1)	344.3	342.34

6-NO2-C-05a	[2-(3,3-Diphenyl-propylsulfanyl)-6-nitro-benzoimidazol-1-yl]-acetic acid	C24H21N3O4S 447.514	7.26 (LC-1)	448.36	446.4
6-NO2-E-03a	[2-(4-Ethyloxycarbonyl-butylsulfanyl)-6-nitro-benzoimidazol-1-yl]-acetic acid	C16H19N3O6S 381.408	6.07 (LC-1)	382.3	380.34
6-NO2-G-06a	{2-[3-(1,3-Dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-6-nitro-benzoimidazol-1-yl}-acetic acid	C20H16N4O6S 440.435	6.11 (LC-1)	441.29	439.4

Table 36

Precursor 5-NO2-C-02b

tert-Butyl (2-benzylsulfanyl-5-nitro-benzoimidazol-1-yl)

A suspension of *tert*-butyl-(2-mercapto-5-nitro-benzoimidazol-1-yl)-acetate (Intermediate **3-IIa**, 31 mg, 0.1 mmol), benzyle bromide (18.8 mg, 13 µl, 0.11 mmol) and K_2CO_3 (28 mg, 0.2 mmol) in acetone (1 ml) is refluxed for 2h 30min. The crude mixture is filtered on a short pad of silica-gel and rinsed with acetone. Evaporation of the solvent *in vacuo* and drying under high *vacuum* yields the title compound as a yellow oil which is used in the next step without further purification: t_R = 7.69 min (LC-1), ESI-MS (pos.): m/z 400.28 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) ($CDCl_3$): 1.33 (s, 9H, *t*Bu), 4.60 (s, 2H), 4.65 (s, 2H), 7.13 (d, 2 H_{arom}), 7.17-7.26 (m, 3 H_{arom}), 7.34 (m, 2 H_{arom}), 8.12 (dd, 1 H_{arom}), 8.55 (d, 1 H_{arom}).

Precursors 5-NO2-C-05b to 6-NO2-G-06b of the following Table 37 are prepared analogous to the procedure described for Precursor 5-NO2-C-02b, using the appropriate alkyl or aryl halogenide for benzyl bromide and the appropriate Intermediate **3-IIa** or Intermediate **3-IIb**, or a (1:1) mixture of both, respectively.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z [M-H]+

5-NO2-C-02b	*tert*-Butyl (2-Benzylsulfanyl-5-nitro-benzoimidazol-1-yl)-acetate	C20H21N3O4S 399.46	7.69 (LC-1)	400.28	n/a
5-NO2-C-05b	*tert*-Butyl [2-(3,3-diphenyl-propylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetate	C28H29N3O4S 503.61	8.42 (LC-1)	504.43	502.47
5-NO2-D-01b	*tert*-Butyl {5-nitro-2-[2-(4-chloro)-phenoxy-ethylsulfanyl]-benzoimidazol-1-yl}-acetate	C21H22ClN3O5S 463.93	8.03 (LC-1)	464.14	462.27
(5/6)-NO2-D-02b	*tert*-Butyl [5-nitro-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetate and its 6-nitro regioisomer	C21H23N3O5S 429.49	7.76 (LC-2)	430.31	428.24
5-NO2-E-03b	*tert*-Butyl [2-(4-ethyloxycarbonyl-butylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetate	C20H27N3O6S 437.51	7.45 (LC-1)	438.35	436.39
5-NO2-G-06b	*tert*-Butyl {2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-5-nitro-benzoimidazol-1-yl}-acetate	C24H24N4O6S 496.54	7.38 (LC-1)	497.36	495.4
5-NO2-H-01b	*tert*-Butyl [2-(3-methoxycarbonyl-benzylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetate	C22H23N3O6S 457.5	2.54 (LC-2)	458.38	456.58
5-NO2-K-01b	*tert*-Butyl {2-[3-(butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-5-nitro-benzoimidazol-1-yl}-acetate	C29H38N4O6S 570.7	8.43 (LC-1)	571.30	569.4
6-NO2-C-02b	*tert*-Butyl (2-benzylsulfanyl-6-nitro-benzoimidazol-1-yl)-acetate	C20H21N3O4S 399.46	7.67 (LC-1)	400.35	n/a
6-NO2-C-05b	*tert*-Butyl [2-(3,3-diphenyl-propylsulfanyl)-6-nitro-benzoimidazol-1-yl]-acetate	C28H29N3O4S 503.61	8.44 (LC-1)	504.33	502.54

6-NO2-D-02b	*tert*-Butyl [6-nitro-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetate	C21H23N3O5S 429.49	7.76 (LC-1)	430.31	428.24
6-NO2-E-03b	*tert*-Butyl [2-(4-ethyloxycarbonyl-butylsulfanyl)-6-nitro-benzoimidazol-1-yl]-acetate	C20H27N3O6S 437.51	7.43 (LC-1)	438.35	436.39
6-NO2-G-06b	*tert*-Butyl {2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-6-nitro-benzoimidazol-1-yl}-acetate	C24H24N4O6S 496.54	7.38 (LC-1)	497.36	495.4

Table 37

Examples H-12a to H-14a of the following Table 38 are prepared analogous to the procedure described for Example H-01a, using Precursors H-12b to H-14b in place of H-01b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^-$
H-12a	[2-(3-Isopropyloxycarbonyl-6-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C21H22N2O5S 414.47	0.86 (LC-3)	415.23	n/a
H-13a	[2-(3-Methyloxycarbonyl-6-phenyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C24H20N2O4S 432.49	1.05 (LC-3)	432.92	431.04
H-14a	[2-(4-Methyloxycarbonyl-oxazol-2-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C15H13N3O5S 347.35	1.70 (LC-2)	347.88	346

Table 38

Precursors H-12b and H-14b of the following Table 39 are prepared using a procedure analogous to that described for Precursor H-01b, using Alkylating agents H-12d and H-14d in place of 5-bromo-hexanoic acid ethyl ester.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
H-12b	*tert*-Butyl [2-(3-isopropyloxycarbonyl-6-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetate	C25H30N2O5S 470.58	2.70 (LC-2)	471.99
H-14b	*tert*-Butyl [2-(4-methyloxycarbonyl-oxazol-2-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate	C19H21N3O5S 403.45	2.24 (LC-2)	403.92

Table 39

Alkylating agent H-12d

3-Chloromethyl-4-methoxy-benzoic acid isopropyl ester

As described in: McKillop, A.; Madjdabadi, F., A.; Long. D. A. Tetrahedron Lett., 1983, 24, 1933-1936.

To a solution of 4-methoxybenzoic acid isopropyl ester (370 mg, 1.89 mmol) in dry nitromethane (10 ml) is added $AlCl_3$ (301 mg, 2.26 mmol, 1.2 eq.) and methoxyacetylchloride (181 µl, 215 mg, 1.98 mmol, 1.05 eq.) and the mixture is stirred overnight at rt. Water (10 ml) is added and the aqueous phase is extracted twice with dichloromethane. The organic phase is dried over Na_2SO_4 and the solvent removed *in vacuo*. The yellowish residue is purified by chromatography on silica-gel (AcOEt / heptane, 1:4), yielding the title compound (87 mg) in 29%: t_R = 2.47 min (LC-2), ESI-MS (pos.): m/z 242.95 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 1.33 (d, 6H, $CH(C\underline{H}_3)_2$), 3.91 (s, 3H, $OC\underline{H}_3$), 4.61 (s, $C\underline{H}_2Cl$), 5.19 (sept., 1H, $C\underline{H}(CH_3)_2$), 6.87 (d, 1 H_{arom}), 7.98 (m, 2 H_{arom}).

Alkylating agent H14-d is prepared accordingly to the described 4 steps procedure: Hermitage, S. A.; Cardwell, K. S.; Chapman, T.; Cooke, J. W. B.; Newton, R. Org. Proc. Res. Development, 2001, 5, 37-44.

Precursor H-13b

tert-Butyl [2-(3-methyloxycarbonyl-6-phenyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetate

To tert-butyl {2-[(6-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetate (Precursor H-08b, 49.1 mg, 0.1 mmol) in 1,2-dimethoxyethane (1.5 ml) are added phenylboronic acid (12.2 mg, 0.1 mmol, 1 eq.), bis(triphenylphosphine)palladium dichloride (0.7 mg, 1 µmol, 1 % mol) and some saturated Na_2CO_3 solution in water (0.3 ml). The resulting biphasic mixture is allowed to stir 25 h at 80°C then 2 h at reflux. Then another load of catalyst is added and the reaction is refluxed overnight. The mixture is allowed to cool down to rt and the solvents are removed *in vacuo*. The yellowish residue is purified twice by chromatography on silica-gel (AcOEt / heptane, 1:4), yielding the title compound (9 mg) in 19% as a colourless oil: t_R = 1.22 min (LC-3), ESI-MS (pos.): m/z 488.98 $[M+H]^+$.

Examples H-15a and H-16a

rac {2-[2-Methoxy-5-(1-methoxy-ethyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid and rac {2-[5-(1-Hydroxy-ethyl)-2-methoxy-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid

To a solution of [2-(5-acetyl-2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid (Example H-11a, 75 mg, 0.2 mmol) in dry methanol (1 ml) is added sodium borohydride (36 mg, 0.92 mmol, 0.46 eq.) and the mixture is stirred at rt for a few minutes. Some 1 N aqueous HCl solution (5 ml) is added and the mixture is extracted three times with AcOEt. The combined organic phase is washed with brine and dried over $MgSO_4$. The solvents are removed under a stream of air to afford a yellowish solid residue which is purified by preparative HPLC yielding: rac {2-[2-methoxy-5-(1-methoxy-ethyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid (4.6 mg) in 6% as a white solid : t_R = 1.70 min (LC-2), ESI-MS (pos.): m/z 385.16 $[M+H]^+$ and rac {2-[5-(1-hydroxy-ethyl)-2-methoxy-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid (2.9 mg) in 4% as a white solid: t_R = 1.73 min (LC-2), ESI-MS (pos.): m/z 372.24 $[M+H]^+$.

Examples (R)-I-01a and (S)-I-01a of the following Table 40 are prepared over two steps analogous to the procedures described for Example I-01a, using Precursors (R)-I-

00b and (S)-I-00b in place of I-00b. They both were purified by preparative thin-layer chromatography on silica-gel: Eluent (Chloroform/ MeOH/ AcOH, 90:10:1).

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
(R)-I-01a	[2-((R)-1-Butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C19H25N3O3S 375.493	0.72 (LC-3)	376.33
(S)-I-01a	[2-((S)-1-Butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C19H25N3O3S 375.494	0.72 (LC-3)	376.33

Table 40

Examples (R)-I-00b and (S)-I-00b of the following Table 41 are prepared analogous to the procedures described for Example I-01b, using (R)-3-hydroxymethyl-piperidine-1-carboxylic acid *tert*-butyl ester or (S)-3-hydroxymethyl-piperidine-1-carboxylic acid *tert*-butyl ester instead of rac 3-hydroxymethyl-piperidine-1-carboxylic acid *tert*-butyl ester.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
(R)-I-00b	*tert*-Butyl [2-((R)-1-*tert*-butyloxycarbonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate	C24H35N3O4S 461.63	1.02 (LC-3)	462.36
(S)-I-00b	*tert*-Butyl [2-((S)-1-*tert*-butyloxycarbonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate	C24H35N3O4S 461.64	1.02 (LC-3)	462.36

Table 41

Example I-14a

rac {2-[1-(3-Phenyl-acryloyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid

rac *tert*-Butyl {2-[1-(2-phenyl-ethenesulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate (Precursor I-14b, 6 mg, 0.011 mmol) in TFA / dichloromethane (1:1, 1 ml) is allowed to stir overnight at rt. The solvents are removed under a stream of air and the resulting product is dried under high vacuum. This yields the title compound (5.6 mg) in 100% as a colourless oil which crystallizes on standing: t_R = 1.06 min (LC-3), ESI-MS (pos.): m/z 471.88 $[M+H]^+$.

Examples I-15a to I-23a of the following Table 42 are prepared analogous to the procedures described for Example I-14a, using Precursors I-15b to I-23b in place of I-14b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
I-15a	rac {2-[1-(3,4-Dichloro-benzenesulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C21H21Cl2N3O4S2 514.45	1.16 (LC-3)	513.84
I-16a	rac [2-(1-Phenylmethanesulfonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C22H25N3O4S2 459.58	1.01 (LC-3)	459.91
I-17a	rac {2-[1-(Toluene-4-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C22H25N3O4S2 459.58	1.06 (LC-3)	459.91
I-18a	rac {2-[1-(Naphthalene-2-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C25H25N3O4S2 495.61	1.12 (LC-3)	495.91
I-19a	rac {2-[1-(Butane-1-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C19H27N3O4S2 425.57	0.98 (LC-3)	425.92
I-20a	rac {2-[1-(4-Methoxy-benzenesulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C22H25N3O5S2 475.58	1.02 (LC-3)	475.9
I-21a	rac {2-[1-(Propane-2-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic	C18H25N3O4S2 411.54	0.89 (LC-3)	411.87

acid

I-22a	rac {2-[1-(Thiophene-2-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C19H21N3O4S3 451.58	1.00 (LC-3)	451.81
I-23a	rac [2-(1-Methanesulfonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C16H21N3O4S2 383.49	0.8 0 (LC-3)	383.91

Table 42

Precursor I-14b

rac *tert*-Butyl {2-[1-(2-phenyl-ethenesulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate

To a solution of DIPEA (63.9 µl, 48.3 mg, 0.37 mmol, 4.5 eq.) and 2-phenyl-ethenesulfonyl chloride (25.2 mg, 0.125 mmol, 1.5 eq.) in 1,2-dichloroethane (0.5 ml) was added 3-(1-*tert*-butoxycarbonylmethyl-1H-benzoimidazol-2-ylsulfanylmethyl)-piperidinium chloride (Intermediate I-00b-bis, 30 mg, 0.083 mmol) in 1,2-dichloroethane (1 ml). The reaction mixture is stirred at rt overnight. The solvents are evaporated under reduced pressure and the crude is purified by preparative HPLC yielding the title compound in 18% as a colourless oil: t_R = 1.20 min (LC-3), ESI-MS (pos.): m/z 528.35 $[M+H]^+$.

Precursors I-15b to I-23b of the following Table 43 are prepared using a procedure analogous to that described for Precursor I-14b, substituting the appropriate sulfonyl chloride for 2-phenyl-ethenesulfonyl chloride

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
I-15b	rac *tert*-Butyl {2-[1-(3,4-dichloro-benzenesulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate	C25H29Cl2N3O4S2 570.55	n/a (LC-3)	n/a	n/a

I-16b	rac *tert*-Butyl [2-(1-phenylmethanesulfonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate	C26H33N3O4S2 515.69	1.18 (LC-3)	516.3	n/a
I-17b	rac *tert*-Butyl {2-[1-(toluene-4-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate	C26H33N3O4S2 515.69	1.21 (LC-3)	516.3	n/a
I-18b	rac *tert*-Butyl {2-[1-(naphthalene-2-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate	C29H33N3O4S2 551.72	1.24 (LC-3)	552.39	550.45
I-19b	rac *tert*-Butyl {2-[1-(butane-1-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate	C23H35N3O4S2 481.67	1.17 (LC-3)	482.3	n/a
I-20b	rac *tert*-Butyl {2-[1-(4-methoxy-benzenesulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate	C26H33N3O5S2 531.69	1.19 (LC-3)	n/a	n/a
I-21b	rac *tert*-Butyl {2-[1-(9ropane-2-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate	C22H33N3O4S2 467.65	1.13 (LC-3)	468.31	n/a
I-22b	rac *tert*-Butyl {2-[1-(thiophene-2-sulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate	C23H29N3O4S3 507.69	1.17 (LC-3)	508.27	n/a
I-23b	rac *tert*-Butyl [2-(1-methanesulfonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate	C20H29N3O4S2 439.59	1.08 (LC-3)	440.26	n/a

Table 43

Intermediate I-00b-bis

3-(1-*tert*-Butoxycarbonylmethyl-1H-benzoimidazol-2-ylsulfanylmethyl)-piperidinium chloride

rac *tert*-Butyl [2-(1-*tert*-butyloxycarbonyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate (Intermediate I-00b, 409 mg, 0.89 mmol) is dissolved in AcOEt / Et_2O (1:1, 4 ml), and 2.2 ml of a 2M HCl solution in Et_2O are added. After 45 min the solvent is removed *in vacuo* and the crude solid formed is dried under high

vacuum, yielding the title compound (360 mg) in 100% as a white solid: t_R = 0.74 min (LC-3), ESI-MS (pos.): m/z 362.31 $[M+H]^+$.

Example I-24a of the following Table 44 is prepared analogous to the procedures described for Example I-01a, using Precursors I-24b in place of I-01b. It is purified by flash-chromatography on silica-gel using (AcOEt/ Acetone/ Water/ Acetic acid) (16:2:1:1) as the eluent.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
I-24a	[2-(1-Butyryl-piperidin-4-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C19H25N3O3S 375.49	2.00 (LC-2)	376.25	374.21

Table 44

Precursor I-24b of the following Table 45 is prepared analogous to the procedures described for Example I-00b, using 4-hydroxymethyl-piperidine-1-carboxylic acid *tert*-butyl ester in place of 3-hydroxymethyl-piperidine-1-carboxylic acid *tert*-butyl ester

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
I-24b	rac *tert*-Butyl [2-(1-*tert*-butyloxycarbonyl-piperidin-4-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate	C24H35N3O4S 461.62	8.95 (LC-1)	462.26

Table 45

Example 5-NO2-H-11a of the following Table 46 is prepared analogous to the procedure described for Example 5-NO2-C-02a, using Precursor 5-NO2-H-11b in place of 5-NO2-C-02b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
5-NO2-H-11a	[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid	C19H17N3O6S 415.42	1.02 (LC-3)	416.06	414.12

Table 46

Precursor 5-NO2-H-11b of the following Table 47 is prepared analogous to the procedure described for Precursor 5-NO2-C-02b, using 1-(3-chloromethyl-4-methoxy-phenyl)-ethanone in place of benzyl bromide.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
5-NO2-H-11b	*tert*-Butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetate	C23H25N3O6S 471.53	1.17 (LC-3)	472.10	470.16

Table 47

Examples 4,6-CF32-H-01a to 5,6-Cl2-I-01a of the following Table 48 are prepared using a procedure analogous to one of those described for Examples (5/6)-Me-D-01a, (5/6)-CN-H-01a, or (5/6)-F-E-03a, using Precursors 4,6-CF32-H-01b to 5,6-Cl2-I-01b in place of (5/6)-Me-D-01b, (5/6)-CN-H-01b, or (5/6)-F-E-03b, respectively.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
4,6-CF32-H-01a	[2-(5-Methyloxycarbonyl-benzylsulfanyl)-4,6-bis-trifluoromethyl-benzoimidazol-1-yl]-acetic acid	C20H14F6N2O4S 492.39	2.60 (LC-2)	492.91
4,6-CF32-H-11a	[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-4,6-bis-trifluoromethyl-benzoimidazol-1-yl]-acetic	C21H16F6N2O4S 506.42	2.55 (LC-2)	506.95

acid

4,6-CF32-I-01a	[2-(1-Butyryl-piperidin-3-ylmethylsulfanyl)-4,6-bis-trifluoromethyl-benzoimidazol-1-yl]-acetic acid	C21H23F6N3O3S 511.48	1.19 (LC-3)	512.04
5,6-Me2-H-01a	[2-(5-Methyloxycarbonyl-benzylsulfanyl)-5,6-dimethyl-benzoimidazol-1-yl]-acetic acid	C20H20N2O4S 384.45	0.98 (LC-3)	384.95
5,6-Me2-H-11a	[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-5,6-dimethyl-benzoimidazol-1-yl]-acetic acid	C21H22N2O4S 398.48	0.96 (LC-3)	399.24
5,6-Me2-I-01a	[2-(1-Butyryl-piperidin-3-ylmethylsulfanyl)-5,6-dimethyl-benzoimidazol-1-yl]-acetic acid	C21H29N3O3S 403.54	0.90 (LC-3)	404.12
5,6-Cl2-H-01a	[2-(5-Methyloxycarbonyl-benzylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetic acid	C18H14Cl2N2O4S 425.29	1.14 (LC-3)	425.02
5,6-Cl2-H-11a	[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetic acid	C19H16Cl2N2O4S 439.31	0.97 (LC-3)	439.1
5,6-Cl2-I-01a	[2-(1-Butyryl-piperidin-3-ylmethylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetic acid	C19H23Cl2N3O3S 444.38	1.09 (LC-3)	443.99

Table 48

Precursors 4,6-CF32-H-01b to 5,6-Cl2-H-11b of the following Table 49 are prepared using a procedure analogous to one of those described for Precursors (5/6)-Me-D-01b, (5/6)-CN-H-01b or (5/6)-F-E-03b, using Intermediates 4,6-CF32-H-01b to 5,6-Cl2-H-11b in place of 5-Me-D-01c, 5-CN-H-01c or 5-F-E-03c.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$

4,6-CF32-H-01b	*tert*-Butyl [2-(5-methyloxycarbonyl-benzylsulfanyl)-4,6-bis-trifluoromethyl-benzoimidazol-1-yl]-acetate	C24H22F6N2O4S 548.50	1.33 (LC-3)	548.95
4,6-CF32-H-11b	*tert*-Butyl [2-(5-Acetyl-2-methoxy-benzylsulfanyl)-4,6-bis-trifluoromethyl-benzoimidazol-1-yl]-acetate	C25H24F6N2O4S 562.52	1.32 (LC-3)	562.94
4,6-CF32-I-01b	*tert*-Butyl [2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-4,6-bis-trifluoromethyl-benzoimidazol-1-yl]-acetate	C25H31F6N3O3S 567.59	1.33 (LC-3)	568.06
5,6-Me2-H-01b	*tert*-Butyl [2-(5-Methyloxycarbonyl-benzylsulfanyl)-5,6-dimethyl-benzoimidazol-1-yl]-acetate	C24H28N2O4S 440.56	1.21 (LC-3)	441.01
5,6-Me2-H-11b	*tert*-Butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-5,6-dimethyl-benzoimidazol-1-yl]-acetate	C25H30N2O4S 454.58	1.17 (LC-3)	454.99
5,6-Me2-I-01b	*tert*-Butyl [2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-5,6-dimethyl-benzoimidazol-1-yl]-acetate	C25H37N3O3S 459.64	1.16 (LC-3)	460.05
5,6-Cl2-H-01b	*tert*-Butyl [2-(5-methyloxycarbonyl-benzylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetate	C22H22Cl2N2O4S 481.39	1.27 (LC-3)	480.88
5,6-Cl2-H-11b	*tert*-Butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetate	C23H24Cl2N2O4S 495.42	1.26 (LC-3)	494.87
5,6-Cl2-I-01b	rac *tert*-Butyl [2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetate	C23H31Cl2N3O3S 500.48	1.26 (LC-3)	499.92

Table 49

Intermediates 4,6-CF32-H-01c to 5,6-Cl2-I-01c of the following Table 50 are prepared using a procedure analogous to one of those described for Intermediates 5-Me-D-01c, 5-CN-H-01c or 5-F-E-03c, using the appropriate 5-substituted benzimidazole-2-thiol in place of 5-methyl-1*H*-benzoimidazole-2-thiol, 5-cyano-1*H*-benzoimidazole-2-thiol or 5-fluoro-1*H*-benzoimidazole-2-thiol, respectively.

Intermediate	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
4,6-CF32-H-01c	4,6-bis-Trifluoromethyl-2-(3-methyloxycarbonyl-benzylsulfanyl)-benzoimidazole	C18H12F6N2O2S 434.36	1.22 (LC-3)	434.85	433.26
4,6-CF32-H-11c	4,6-bis-Trifluoromethyl-2-(3-acetyl-6-methoxybenzylsulfanyl)-benzoimidazole	C19H14F6N2O2S 448.38	1.21 (LC-3)	448.83	447.17
4,6-CF32-I-01c	rac 4,6-Bis-trifluoromethyl-2-(1-butanoyl-piperidin-3-ylmethylsulfanyl)-benzoimidazole	C19H21F6N3OS 453.44	1.19 (LC-3)	453.89	453.26
5,6-Me2-H-01c	5,6-Dimethyl-2-(3-methyloxycarbonyl-benzylsulfanyl)-benzoimidazole	C18H18N2O2S 326.41	0.93 (LC-3)	326.91	325.11
5,6-Me2-H-11c	5,6-Dimethyl-2-(3-acetyl-6-methoxybenzylsulfanyl)-benzoimidazole	C19H20N2O2S 340.44	0.88 (LC-3)	340.95	339.22
5,6-Me2-I-01c	rac 5,6-Dimethyl-2-(1-butanoyl-piperidin-3-ylmethylsulfanyl)-benzoimidazole	C19H27N3OS 345.50	0.85 (LC-3)	346	344.27
5,6-Cl2-H-01c	5,6-dichloro-2-(3-methyloxycarbonyl-benzylsulfanyl)-benzoimidazole	C16H12Cl2N2O2S 367.25	0.93 (LC-3)	326.91	325.11
5,6-Cl2-H-11c	5,6-dichloro-2-(3-acetyl-6-methoxybenzylsulfanyl)-benzoimidazole	C17H14Cl2N2O2S 381.28	1.14 (LC-3)	380.87	n/a
5,6-Cl2-I-01c	rac 5,6-Dichloro-2-(1-butanoyl-piperidin-3-ylmethylsulfanyl)-benzoimidazole	C17H21Cl2N3OS 386.34	1.1 (LC-3)	385.92	n/a

Table 50

Example 5-HCO-H-11a

[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-5-formyl-benzoimidazol-1-yl]-acetic acid

A solution of *tert*-butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-formyl-benzoimidazol-1-yl]-acetate (Precursor 5-HCO-H-11b, 16 mg, 0.035 mmol) in TFA /

dichloromethane (1:1, 4 ml) is allowed to stir overnight at rt. The solvents are removed under a stream of air and the resulting products are dried under high vacuum. This yields the title compound (14 mg) in 100% as a yellow solid: t_R = 0.94 min (LC-3), ESI-MS (pos.): m/z 398.86 $[M+H]^+$, ESI-MS (neg.): m/z 397.06 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 2.46 (s, 3H, $COCH_3$), 3.88 (s, 3H, OCH_3), 4.59 (s, 2H, SCH_2), 4.96 (s, 2H, CH_2CO_2), 7.11 (d, 1 H_{arom}), 7.65 (d, 1 H_{arom}), 7.74 (d, 1 H_{arom}), 7.90 (dd, 1 H_{arom}), 8.06 (d, 1 H_{arom}), 8.12 (d, 1 H_{arom}), 10.01 (s, 1H, CHO).

Examples 5,6-F2-H-11a to 5-F-H-11a of the following Table 51 are prepared analogous to the procedure described for Example 5-HCO-H-11a, using Precursors 5,6-F2-H-11b to 5-F-H-11b in place of 5-HCO-H-11b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
5,6-F2-H-11a	[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-5,6-difluoro-benzoimidazol-1-yl]-acetic acid	C19H16F2N2O4S 406.40	1.01 (LC-2)	406.96	405.09
5-MeSO2-H-11a	[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-5-methanesulfonyl-benzoimidazol-1-yl]-acetic acid	C20H20N2O6S2 448.51	0.91 (LC-3)	448.83	447.03
5-MeCO-H-11a	[5-Acetyl-2-(5-acetyl-2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C21H20N2O5S 412.46	0.94 (LC-3)	412.84	411.04
4-F-H-11a	[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-4-fluoro-benzoimidazol-1-yl]-acetic acid	C19H17FN2O4S 388.41	0.99 (LC-3)	388.83	387.03
5-CF3-H-11a	[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetic acid	C20H17F3N2O4S 438.42	1.07 (LC-3)	438.86	437.06
5-F-H-11a	[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid	C19H17FN2O4S 388.41	0.96 (LC-3)	388.94	387.08

Table 51

Example 6-F-H-11a

[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-6-fluoro-benzoimidazol-1-yl]-acetic acid

To a solution of methyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-6-fluoro-benzoimidazol-1-yl]-acetate (Precursor 6-F-H-11b, 11.3 mg, 0.029 mmol) in dry THF (0.3 ml) is added some 1 N aqueous lithium hydroxide solution (0.140 ml, 5 eq.). The resulting biphasic solution is allowed to stir 1 h at rt. The solvents are removed *in vacuo*, water is added as well as 1N HCl in water so as to set the pH of the aqueous solution to pH=1. The resulting acidic aqueous phase is extracted three times with AcOEt. The organic phase is dried over Na_2SO_4 and the solvent removed *in vacuo* and the product was dried under high vacuum. This yields the title compound (6 mg) in 55% as a greyish solid: t_R = 0.95 min (LC-3), ESI-MS (pos.): m/z 388.89 $[M+H]^+$, ESI-MS (neg.): m/z 387.10 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 2.40 (s, 3H, $COCH_3$), 3.87 (s, 3H, OCH_3), 4.49 (s, 2H, SCH_2), 4.82 (s, 2H, CH_2CO_2), 7.01 (t, 1 H_{arom}), 7.09 (d, 1 H_{arom}), 7.42 (d, 1 H_{arom}), 7.53 (dd, 1 H_{arom}), 7.86 (d, 1 H_{arom}), 7.98 (s, 1 H_{arom}).

Example 5-F-H-11a (1'-Me) of the following Table 52 is prepared analogous to the procedure described for Example 6-F-H-11a, using Precursor 5-F-H-11b (1'-Me) in place of 6-F-H-11b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
5-F-H-11a (1'-Me)	rac 2-[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-propionic acid	C20H19FN2O4S 402.44	1.00 (LC-3)	402.87	401.07

Table 52

Precursors 5-HCO-H11b to 5-F-H-11b (1'-Me) of the following Table 53 are prepared using a procedure analogous to that described for Precursor H-01b, substituting 1-(3-chloromethyl-4-methoxy-phenyl)-ethanone for 5-bromo-hexanoic acid ethyl ester and using Intermediates 3-III to 3-IXbis for Intermediate 3-I.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^-$
5-HCO-H-11b	*tert*-Butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-formyl-benzoimidazol-1-yl]-acetate	C24H26N2O5S 454.54	1.13 (LC-3)	454.92	n/a
5,6-F2-H-11b	*tert*-Butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-5,6-difluoro-benzoimidazol-1-yl]-acetate	C23H24F2N2O4S 462.51	1.06 (LC-3)	463.32	n/a
5-MeSO2-H-11b	*tert*-Butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-methanesulfonyl-benzoimidazol-1-yl]-acetate	C24H28N2O6S2 504.62	1.08 (LC-3)	504.91	503.25
5-MeCO-H-11a	*tert*-Butyl [5-acetyl-2-(5-acetyl-2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetate	C25H28N2O5S 468.57	1.13 (LC-3)	468.98	n/a
4-F-H-11b	*tert*-Butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-4-fluoro-benzoimidazol-1-yl]-acetate	C23H25FN2O4S 444.52	1.16 (LC-3)	444.89	n/a
5-CF3-H-11b	*tert*-Butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetate	C24H25F3N2O4S 494.53	1.21 (LC-3)	494.94	n/a
5-F-H-11b	*tert*-Butyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate	C23H25FN2O4S 444.52	1.16 (LC-3)	445.03	n/a
6-F-H-11b	Methyl [2-(5-acetyl-2-methoxy-benzylsulfanyl)-6-fluoro-benzoimidazol-1-yl]-acetate	C20H19FN2O4S 402.44	1.06 (LC-3)	402.87	n/a
5-F-H-11a (1'-Me)	Ethyl 2-[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-propionate	C22H23FN2O4S 430.49	1.12 (LC-3)	430.97	n/a

Table 53

Intermediate 3-VIII

tert-Butyl (2-mercapto-5-trifluoromethyl-benzoimidazol-1-yl)-acetate

In a test tube equipped with a septum, *tert*-butyl (2-nitro-4-trifluoromethyl-phenylamino)-acetate (Starting material 5-VIII, 80 mg, 0.25 mmol) is dissolved in dry THF (0.5 ml). Argon is allowed to bubble through this solution for 10 min. Then dry

palladium on carbon (10% w/w, 26 mg, 10% mol) is added and the flask is set under H_2 atmosphere. The resulting mixture is shaken vigorously at rt overnight. If necessary, another 8% mol of palladium on charcoal 10% w/w is added and the resulting suspension is stirred for another hour under H_2 atmosphere. The crude mixture is then filtered over celite to remove any solid particle. The celite is rinsed once with dry THF. To the resulting light yellow solution is added, under argon, 1,1'-thiocarbonyldiimidazole (89 mg, 0.5 mmol, 2 eq.). The resulting orange solution is allowed to stir at rt for 5 h. Water is then added. The yellow solid formed is filtered over a fritted funnel, rinsed thoroughly with water and dried under high vacuum. This yields the title compound (60 mg) in 73% as a yellow solid: t_R = 1.10 min (LC-3), ESI-MS (pos.): m/z 332.99 $[M+H]^+$, 331.13 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.41 (s, 9H, *t*Bu), 5.06 (s, 2H, $NHC\underline{H}_2CO_2$), 7.44 (s, 1H, H_{arom}), 7.57 (s, 2H, H_{arom}), 13.25 (br. s, 1H, SH).

Intermediates 3-III to 3-IXbis of the following Table 54 are prepared using a procedure analogous to that described for Intermediate 3-VIII, using Starting materials 5-III to 5-IXbis in place of Starting material 5-VIII.
In some cases the product was purified by flash-chromatography on silica-gel using a suitable (AcOEt / heptane) mixture [(3:7), (4:6) or (5:5)] as the eluent.

Intermediate	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
3-III	tert-Butyl (5-formyl-2-mercapto-benzoimidazol-1-yl)-acetate	C14H16N2O3S 292.35	1 (LC-3)	n/a	291.15
3-IV	tert-Butyl (5,6-difluoro-2-mercapto-benzoimidazol-1-yl)-acetate	C13H14F2N2O2S 300.32	1.21 (LC-3)	n/a	299.17
3-V	tert-Butyl (2-mercapto-5-methanesulfonyl-benzoimidazol-1-yl)-acetate	C14H18N2O4S2 342.43	0.97 (LC-3)	342.82	341.16
3-VI	tert-Butyl (5-acetyl-2-mercapto-benzoimidazol-1-yl)-acetate	C15H18N2O3S 306.38	1 (LC-3)	n/a	305.12

3-VII	tert-Butyl (4-fuoro-2-mercapto-benzoimidazol-1-yl)-acetate	C13H15FN2O2S 282.33	1.03 (LC-3)	n/a	281.13
3-IX	*tert*-Butyl (5-fluoro-2-mercapto-benzoimidazol-1-yl)-acetate	C13H15FN2O2S 282.33	1.05 (LC-2)	n/a	281.13
3-X	Methyl (6-fluoro-2-mercapto-benzoimidazol-1-yl)-acetate	C10H9FN2O2S 240.25	0.9 (LC-3)	240.89	239.17
3-IXbis	rac Ethyl 2-(5-fluoro-2-mercapto-benzoimidazol-1-yl)-propionate	C12H13FN2O2S 268.31	0.99 (LC-3)	268.99	267.09

Table 54

Starting material 5-VIII

tert-Butyl (2-nitro-4-trifluoromethyl-phenylamino)-acetate

A mixture of 4-fluoro-3-nitrobenzotrifluoride (209 mg, 1 mmol), glycine *tert*-butyl ester hydrochloride (201 mg, 1.2 mmol) and $NaHCO_3$ (128 mg, 2 mmol) in dry DMSO (1 ml) is stirred overnight at 50 or 65°C. In case the reaction is not complete a further heating at 85°C to 100°C for 3 h is necessary. The reaction is then cooled to rt and water is added. The yellow to orange solid formed is filtered over a fritted funnel, rinsed thoroughly with water and dried under high vacuum. This yields the title compound (254 mg) in 79% as a yellow solid: t_R = 1.08 min (LC-3), ESI-MS (pos.): m/z 403.2 $[M+2AcCN]^+$, m/z 321.56 $[M+H]^+$, ^{1}H-NMR (DMSO-d_6): δ (ppm) 1.44 (s, 9H, *t*Bu), 4.23 (d, 2H, $NHC\underline{H}_2CO_2$), 7.08 (d, 1H, H_{arom}), 7.80 (dd, 1H, H_{arom}), 8.34 (br. s, 1H, H_{arom}), 8.65 (t, 1 H, N<u>H</u>).

Starting materials 5-III to 5-IXbis of the following Table 55 are prepared using a procedure analogous to that described for Starting material 5-V, substituting the appropriate *o*-nitrofluorobenzene for 4-fluoro-3-nitrobenzotrifluoride and the appropriate amino-acid ester hydrochloride for glycine *tert*-butyl ester hydrochloride. In some cases the product is purified by recrystallization out of a heptane / toluene (1:1) mixture or by flash-chromatography on silica gel using a heptane / AcOEt (4:1) mixture as eluent.

Starting material	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
5-III	*tert*-Butyl (4-formyl-2-nitro-phenylamino)-acetate	C13H16N2O5 280.28	1.09 (LC-3)	n/a	279.33
5-IV	*tert*-Butyl (4,5-difluoro-2-nitro-phenylamino)-acetate	C12H14F2N2O4 288.25	1.09 (LC-3)	n/a	287.14
5-V	*tert*-Butyl (4-methanesulfonyl-2-nitro-phenylamino)-acetate	C13H18N2O6S 330.36	1.04 (LC-3)	n/a	329.19
5-VI	*tert*-Butyl (4-acetyl-2-nitro-phenylamino)-acetate	C14H18N2O5 294.30	1.1 (LC-3)	294.89	n/a
5-VII	*tert*-Butyl (3-fluoro-2-nitro-phenylamino)-acetate	C12H15FN2O4 270.26	1.01 (LC-3)	n/a	n/a
5-IX	tert-Butyl (4-fluoro-2-nitro-phenylamino)-acetate	C12H15FN2O4 270.26	1.03 (LC-3)	271.21	n/a
5-X	Methyl (5-fluoro-2-nitro-phenylamino)-acetate	C9H9FN2O4 228.18	1.94 (LC-2)	228.8	227.2
5-IXbis	rac Ethyl 2-(4-Fluoro-2-nitro-phenylamino)-propionate	C11H13FN2O4 256.23	1.14 (LC-3)	271.03	n/a

Table 55

Example 5-F-H-17a

{2-[5-(2,3-Dihydro-indole-1-carbonyl)-2-methoxy-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid

tert-Butyl {2-[5-(2,3-dihydro-indole-1-carbonyl)-2-methoxy-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetate (Precursor 5-F-H-17b, 26 mg, 0.047 mmol) in a TFA / dichloromethane mixture (1:1, 0.5 ml) is allowed to stir at rt for 4 h. The solvents are removed under a stream of air. The product is precipitated in Et_2O, filtered, rinsed with

Et_2O and dried under high vacuum. This yields the title compound (22 mg) in 99% as a light pink solid: t_R = 1.04 min (LC-3), ESI-MS (pos.): m/z 492.11 $[M+H]^+$, ESI-MS (neg.): m/z 490.18 $[M-H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 2.88 (t, 2H, $NCH_2\underline{CH_2}Ar$), 3.85 (t, 2H, NCH_2CH_2Ar), 3.89 (s, 3H, OCH_3), 4.54 (s, 2H, SCH_2), 4.95 (s, 2H, CH_2CO_2), 6.97 (t, 1 H_{arom}), 7.02-7.09 (m, 4 H_{arom}), 7.11 (d, 1 H_{arom}), 7.21 (d, 1 H_{arom}), 7.38-7.57 (m, 3 H_{arom}).

Examples 5-F-H-18a to 5-F-H-29a of the following Table 56 are prepared analogous to the procedure described for Example 5-F-H-17a, using Precursors 5-F-H-18b to 5-F-H-29b in place of 5-F-H-17b. In some cases purification must be carried out by preparative HPLC.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
5-F-H-18a	[2-(5-Butylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid	C22H24FN3O4S 445.51	1.00 (LC-3)	446.12	444.18
5-F-H-19a	{2-[2-Methoxy-5-(morpholine-4-carbonyl)-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid	C22H22FN3O5S 459.49	0.88 (LC-3)	460.18	458.17
5-F-H-20a	[2-(5-Benzylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid	C25H22FN3O4S 479.52	1.01 (LC-3)	480.13	478.19
5-F-H21a	[2-(5-Diethylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid	C22H24FN3O4S 445.51	0.96 (LC-3)	446.19	444.18
5-F-H22a	{2-[5-(Benzyl-ethyl-carbamoyl)-2-methoxy-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid	C27H26FN3O4S 507.58	1.04 (LC-3)	508.19	506.25
5-F-H23a	[2-(5-Acetyl-2-ethoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid	C20H19FN2O4S 402.44	1.01 (LC-3)	403.04	401.1
5-F-H-24a	{2-[5-Acetyl-2-(3-hydroxy-propoxy)-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid	C21H21FN2O5S 432.47	1.48 (LC-3)	433.3	431.16

5-F-H-25a	[2-(5-Acetyl-2-propoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid	C21H21FN2O4S 416.47	1.05 (LC-3)	417.1	415.16
5-F-H26a	[2-(5-Acetyl-2-butoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid	C22H23FN2O4S 430.49	1.09 (LC-3)	431.06	429.15
5-F-H27a	[2-(5-Benzoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid	C24H19FN2O4S 450.48	1.07 (LC-3)	451.04	448.96
5-F-H28a	[5-Fluoro-2-(6-methoxy-3-oxo-indan-5-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C20H17FN2O4S 400.42	0.96 (LC-3)	401.04	399.1
5-F-H29a	[5-Fluoro-2-(3-methoxy-8-oxo-5,6,7,8-tetrahydro-naphthalen-2-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C21H19FN2O4S 414.45	1.00 (LC-3)	415.03	413.09

Table 56

5-F-H-17b

tert-Butyl {2-[5-(2,3-dihydro-indole-1-carbonyl)-2-methoxy-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetate

To a solution of *tert*-butyl [2-(3-hydroxycarbonyl-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate (Precursor 5-F-H-00b, 44.6 mg, 0.1 mmol) in dry DMF (0.8 ml) are added successively Et_3N (21.1 µl, 15.2 mg, 0.15 mmol, 1.5 eq.), HOBt (23.0 mg, 0.15 mmol, 1.5 eq.), N-(3-dimethylaminopropyl)-N'-ethylcarbodiimide hydrochloride (28.8 mg, 0.15 mmol, 1.5 eq.) and indoline (16.8 µl, 17.9 mg, 0.15 mmol, 1.5 eq.). The reaction mixture is stirred at rt overnight. The solvents are evaporated under reduced pressure, dichloromethane (4 ml) is added and the resulting organic phase is washed once with 2 ml of a 1M $NaHCO_3$ solution in water and once with 2 ml of a 1M solution of sodium hydrogen sulfate in water. The acidic aqueous phase was extracted once with dichloromethane (2 ml). The combined organic phase is washed with brine. The solvent is removed under a stream of air and the resulting crude product is dried under high vacuum overnight yielding the title compound (40 mg) in 83% as a light brown oil: t_R = 1.20 min (LC-3), ESI-MS (pos.): m/z 548.23 $[M+H]^+$,

^{1}H-NMR ($CDCl_3$): δ (ppm) 1.400 (s, 9H, *t*Bu), 2.95 (t, 2H, $NCH_2\underline{CH_2}Ar$), 3.91 (s, 3H, OCH_3), 3.95 (t, 2H, $NC\underline{H_2}CH_2Ar$), 4.65 (s, 2H, SCH_2), 4.72 (s, 2H, CH_2CO_2), 6.91-7.19 (m, 7 H_{arom}), 7.45 (m, 1 H_{arom}), 7.52 (m, 1 H_{arom}), 7.64 (m, 1 H_{arom}).

Precursors 5-F-H-18b to 5-F-H22b of the following Table 57 are prepared using a procedure analogous to that described for Precursor 5-F-H-17b, substituting the appropriate sulfonyl chloride for 2-phenyl-ethenesulfonyl chloride.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
5-F-H-18b	*tert*-Butyl [2-(5-butylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate	C26H32FN3O4S 501.61	1.16 (LC-3)	502.23	500.23
5-F-H-19b	*tert*-Butyl {5-fluoro-2-[2-methoxy-5-(morpholine-4-carbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetate	C26H30FN3O5S 515.60	1.09 (LC-3)	516.29	514.56
5-F-H-20b	*tert*-Butyl [2-(5-benzylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate	C29H30FN3O4S 535.63	1.17 (LC-3)	536.24	534.23
5-F-H21b	*tert*-Butyl [2-(5-diethylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate	C26H32FN3O4S 501.61	1.14 (LC-3)	502.3	n/a
5-F-H22b	*tert*-Butyl {2-[5-(benzyl-ethyl-carbamoyl)-2-methoxy-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetate	C31H34FN3O4S 563.68	1.21 (LC-3)	564.30	n/a

Table 57

Precursor 5-F-H-00b

tert-Butyl [2-(3-hydroxycarbonyl-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate

To a solution of 3-hydroxymethyl-4-methoxy-benzoic acid (Starting material H-00e, 910 mg, 5 mmol) in dry THF (50 ml) cooled to 0°C under inert atmosphere are added successively triphenylphosphine (1782 mg, 6 mmol, 1.2 eq.) and di-*tert*-butyl-azodicarboxylate (1381 mg, 6 mmol, 1.2 eq). The initially deep yellow colour disappears after 10 min. Then *tert*-butyl (5-fluoro-2-mercapto-benzoimidazol-1-yl)-

acetate (Intermediate 3-III, 1270 mg, 0.9 mmol, 0.9 eq.) is added. The reaction mixture is allowed to warm up to rt and stirred at this temperature for 1 h. Evaporation of the solvent *in vacuo* and purification by flash-chromatography on silica gel (AcOEt / heptane/ AcOH, 10:90:1), provides the title compound (680 mg) in 30% as beige solid: t_R = 1.08 min (LC-3), ESI-MS (pos.): m/z 447.09 $[M+H]^+$, ESI-MS (neg.): m/z 426.18 $[M-H]^+$.

Starting material H-00e

3-Hydroxymethyl-4-methoxy-benzoic acid

Onto a warm solution of $Ca(OCl)_2$ (7.14 g, 49.95 mmol, 3.3 eq.) in water (25 ml) is added a warm solution of K_2CO_3 (5.14 g, 37.35 mmol, 2.49 eq.) and KOH (1.46 g, 26.1 mmol, 1.74 eq.) in water (25 ml) . After 30 min of vigourous stirring, the undesired solid formed is filtered and rinsed with little water. The solution obtained is poured onto a suspension of 1-(3-chloromethyl-4-methoxy-phenyl)-ethanone (2.98 g, 15 mmol) in 1,4-dioxane (10 ml). The resulting suspension is stirred 2 h at rt and 2 h at 70°C.Under cooling of the suspension in an ice bath, are subsequently added solid $NaHSO_3$ (100 mg), then 96% sulfuric acid until pH = 3. The aqueous phase thus obtained is extracted four times with AcOEt. The combined organic phase is washed with brine and dried over Na_2SO_4. Evaporation of the solvent *in vacuo* yields the title compound (1.8 g) in 66% as a white solid. t_R = 0.72 min (LC-3), ESI-MS (pos.): m/z 182.99 $[M+H]^+$.

Precursors 5-F-H-23b to 5-F-H-29b of the following Table 58 are prepared using a procedure analogous to that described for Precursor H-01b, using Alkylating agents H-23d to H-29d in place of 5-bromo-hexanoic acid ethyl ester.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
5-F-H23b	*tert*-Butyl [2-(5-acetyl-2-ethoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate	C24H27FN2O4S 458.55	1.18 (LC-3)	459.14

5-F-H-24b	*tert*-Butyl {2-[5-acetyl-2-(3-hydroxy-propoxy)-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetate	C25H29FN2O5S 488.57	1.08 (LC-3)	489.07
5-F-H-25b	*tert*-Butyl [2-(5-acetyl-2-propoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate	C25H29FN2O4S 472.57	1.22 (LC-3)	473.20
5-F-H26b	*tert*-Butyl [2-(5-acetyl-2-butoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate	C26H31FN2O4S 486.60	1.24 (LC-3)	487.13
5-F-H27b	*tert*-Butyl [2-(5-benzoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate	C28H27FN2O4S 506.59	1.22 (LC-3)	507.22
5-F-H28b	*tert*-Butyl [5-fluoro-2-(6-methoxy-3-oxo-indan-5-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate	C24H25FN2O4S 456.53	1.16 (LC-3)	457.14
5-F-H29b	*tert*-Butyl [5-fluoro-2-(3-methoxy-8-oxo-5,6,7,8-tetrahydro-naphthalen-2-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate	C25H27FN2O4S 470.56	1.17 (LC-3)	471.20

Table 58

Alkylating agents H-23d to H-29d of the following Table 59 are prepared using a procedure analogous to that described for Alkylating agent H-12d, substituting the corresponding reagent or H-24g for 4-methoxybenzoic acid isopropyl ester.

Alkylating agent	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
H-23d	1-(3-Chloromethyl-4-ethoxy-phenyl)-ethanone	C11H13ClO2 212.67	1.07 (LC-3)	213.09
H-24d	1-[3-Chloromethyl-4-(3-hydroxy-propoxy)-phenyl]-ethanone	C12H15ClO3 242.70	0.92 (LC-3)	243.05
H-25d	1-(3-Chloromethyl-4-propoxy-phenyl)-ethanone	C12H15ClO2 226.70	1.11 (LC-3)	227.13

H-26d	1-(3-Chloromethyl-4-butoxy-phenyl)-ethanone	C13H17ClO2 240.73	1.15 (LC-3)	241.11
H-27d	(3-Chloromethyl-4-methoxy-phenyl)-phenyl-methanone	C15H13ClO2 260.72	1.01 (LC-3)	261.11
H-28d	6-Chloromethyl-5-methoxy-indan-1-one	C11H11ClO2 210.66	0.99 (LC-3)	211.08
H-29d	7-Chloromethyl-6-methoxy-3,4-dihydro-2H-naphthalen-1-one	C12H13ClO2 224.68	1.04 (LC-3)	225.06

Table 59

Starting material H-24g

1-[4-(3-Hydroxy-propoxy)-phenyl]-ethanone

is prepared according to the procedure described in: Mandoli, A.; Calamante, M.; Feringa, B. L.; Salvadori, P. Tetrahedron Asymmetry 2003, 14, 3647-3650.

Examples 5-F-I-01a to 5-F-I-35a of the following Table 60 are prepared analogous to the second procedure described for the synthesis of Example I-01a, using Precursors 5-F-I-01b to 5-F-I-35b in place of 5-F-H-17b. The products which did not crystallize were pure enough to be used as such in the next step.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
5-F-I-01a	rac [2-(1-Butyryl-piperidin-3-ylmethylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid	C19H24FN3O3S 393.48	0.92 (LC-3)	394.02	392.22
5-F-I-11a	rac {5-Fluoro-2-[1-(furan-2-carbonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C20H20FN3O4S 417.45	0.94 (LC-3)	417.89	416.16

5-F-I-13a	rac {2-[1-(4-Bromo-benzoyl)-piperidin-3-ylmethylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid	C22H21BrFN3O3S 506.39	1.01 (LC-3)	507.89	506.09
5-F-I-34a	(S)-[5-Fluoro-2-(1-benzyloxycarbonyl-azetidin-2-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C21H20FN3O4S 429.46	1.02 (LC-3)	430.12	428.18
5-F-I-35a	[5-Fluoro-2-(1-benzyloxycarbonyl-azetidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C21H20FN3O4S 429.46	1.01 (LC-3)	429.98	428.11

Table 60

Precursor 5-F-I-01b

rac *tert*-Butyl [2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate

To a solution of 1-(3-hydroxymethyl-piperidin-1-yl)-butan-1-one (Starting material I-01e, 278 mg, 1.5 mmol, 1.5 eq.) in dry THF (10 ml) cooled to 0°C under inert atmosphere are added successively triphenylphosphine (458 mg, 1.75 mmol, 1.75 eq.) and di-*tert*-butyl-azodicarboxylate (402 mg, 1.75 mmol, 1.75 eq). The initially deep yellow colour disappears after 10 min. Then *tert*-butyl (5-fluoro-2-mercapto-benzoimidazol-1-yl)-acetate (Intermediate 3-III, 280 mg, 1 mmol) is added. The reaction mixture is slowly allowed to warm up to rt overnight. Evaporation of the solvent *in vacuuo* and purification by flash-chromatography on silica gel (AcOEt / heptane, 2:3), provides the title compound (217 mg) in 95% as a slightly yellow resin: t_R = 1.14 min (LC-3), ESI-MS (pos.): m/z 450.08 $[M+H]^+$.

Precursors 5-F-I-11b to 5-I-35b of the following Table 61 are prepared using a procedure analogous to that described for Precursor 5-F-I-01b, using Starting material I-11e to I-35e in place of Starting material I-01e.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$

5-F-I-11b	rac *tert*-Butyl {5-fluoro-2-[1-(furan-2-carbonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate	C24H28FN3O4S 473.56	1.19 (LC-3)	474.03
5-F-I-13b	rac *tert*-Butyl {2-[1-(4-bromo-benzoyl)-piperidin-3-ylmethylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetate	C26H29BrFN3O3S 562.49	1.18 (LC-3)	563.98
5-F-I-34b	(S)-*tert*-Butyl [5-Fluoro-2-(1-benzyloxycarbonyl-azetidin-2-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate	C25H28FN3O4S 485.57	1.19 (LC-3)	485.98
5-F-I-35b	*tert*-Butyl [5-fluoro-2-(1-benzyloxycarbonyl-azetidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetate	C25H28FN3O4S 485.57	1.16 (LC-3)	486.02

Table 61

Starting materials I-11e and I-13e of the following Table 62 are prepared using a procedure analogous to that described for Starting material I-01e, substituting the corresponding acid chloride to butyryl chloride.

Starting material	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
I-11e	Furan-2-yl-(3-hydroxymethyl-piperidin-1-yl)-methanone	C11H15NO3 209.24	0.62 (LC-3)	210.15
I-13e	(4-Bromo-phenyl)-(3-hydroxymethyl-piperidin-1-yl)-methanone	C13H16BrNO2 298.18	0.77 (LC-3)	298.1

Table 62

Starting material I-34e

(S)-2-Hydroxymethyl-azetidine-1-carboxylic acid benzyl ester

To a solution of (S)-Azetidine-1,2-dicarboxylic acid 1-benzyl ester (Starting material I-34f, 94 mg, 0.4 mmol) in 0.3 ml dry THF cooled to 0°C is added dropwise 450 µl of a 1M solution of borane in THF. The resulting solution is allowed to stir for 1 h at 0°C

and warm up to rt overnight. AcOH (1 ml) and water (1 ml) are then added as well as some saturated $NaHCO_3$ solution in water until pH=9 and no more gas evolution occurs. The resulting aqueous phase is extracted three times with AcOEt. The combined organic phase is washed once with some saturated $NaHCO_3$ solution in water and once with water. The solvents are evaporated *in vacuo* and the crude oil dried under high vacuum overnight, yielding the title compound (79 mg) in 89% as a colourless oil: t_R = 0.84 min (LC-3), ESI-MS (pos.): m/z 222.08 $[M+H]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.00 (m, 1H, $C\underline{H_2}CH_2N$), 2.22 (m, 1H, $C\underline{H_2}CH_2N$), 3.78-4.01 (m, 5H, $C\underline{H_2}N$ and $C\underline{H_2}O\underline{H}$), 4.52 (s, 2 H, $OC\underline{H_2}Ph$), 7.35 (s, 5 H, $H_{arom.}$).

Starting material I-35e of the following Table 63 is prepared using a procedure analogous to that described for Starting material I-34e, substituting Starting material I-35f for I-34f.

Starting material	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
I-35e	3-Hydroxymethyl-azetidine-1-carboxylic acid benzyl ester	C12H15NO3 221.26	0.87 (LC-3)	222.22

Table 63

Starting material I-34f

(S)-Azetidine-1,2-dicarboxylic acid 1-benzyl ester

To a solution of L-azetidine-2-carboxylic acid (101.1 mg, 1 mmol) in 2N aqueous NaOH (0.675 ml) is added benzylchloroformiate (169 µl, 204.7 mg, 1.2 eq.) and the resulting mixture is stirred at rt for 2 h. The aqueous phase is washed once with Et_2O. The aqueous solution is set to pH=2 with a concentrated aqueous HCl solution and then saturated with solid Na_2SO_4. It is extracted three times with AcOEt. The combined organic phase is dried over Na_2SO_4. The solvents are evaporated under a stream of air and the crude oil dried under high vacuum overnight, yielding the title compound (126 mg) in 53% as a colourless oil: t_R = 0.76 min (LC-3), ESI-MS (pos.): m/z 277.16

$[M+Na]^+$; ^{1}H-NMR ($CDCl_3$): δ (ppm) 2.53 (bs, 2H, $C\underline{H}_2CH_2N$), 4.01 (t, 2H, $CH_2\underline{N}$), 4.82 (t, 1 H, $C\underline{H}CO_2H$), 5.15 (s, 2H, $OC\underline{H}_2Ph$), 7.35 (s, 5 H, $H_{arom.}$).

Starting material I-35f of the following Table 64 is prepared using a procedure analogous to that described for Starting material I-34f, substituting 3-azetidine carboxylic acid for L-azetidine-2-carboxylic acid.

Intermediate	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
I-35f	Azetidine-1,3-dicarboxylic acid monobenzyl ester	C12H13NO4 235.25	0.75 (LC-3)	236.14

Table 64

Example 5-F-I-29a

rac [5-Fluoro-2-(1-phenylacetyl-pyrrolidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid

rac [2-(Pyrrolidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid (Precursor 5-F-I-36a, 17.3 mg, 0.05 mmol) is suspended in dichloromethane (1 ml) and Et_3N (10.2 mg, 14.3 µl, 0.1 mmol, 2 eq.) as well as phenylacetyl chloride (9.28 mg, 8.00 µl, 0.06 mmol, 1.2 eq.) are added subsequently. The resulting mixture is stirred for 1 h at rt. Some 1N aqueous NaOH solution (1 ml) was added and the mixture is allowed to stir at rt for 1 h. Then dichloromethane (1 ml) and water (1 ml) are added and the aqueous solution is washed twice with dichloromethane to remove non-acidic impurities. The combined organic phase is washed with brine. Both aqueous phases (basic + brine) are then made acidic with 1 ml AcOH and the crude acid is extracted twice with dichloromethane (2 ml). The combined organic phases are washed with brine and dried over Na_2SO_4. Evaporation of the solvent *in vacuo* and drying under high *vacuum*, yields the title compound (15 mg) in 68% as a white solid: t_R = 0.94 min (LC-2), ESI-MS (pos.): m/z 428.11 $[M+H]^+$, ESI-MS (neg.): m/z 426.18 $[M-H]^+$.

Examples 5-F-I-25a to 5-F-I-33a of the following Table 65 are prepared analogous to the procedures described for 5-F-I-29a, substituting the corresponding acid chloride or sulfonyl chloride for phenylacetyl chloride.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$	MS Data m/z $[M-H]^+$
5-F-I-25a	rac {2-[1-(4-Bromo-benzoyl)-pyrrolidin-3-ylmethylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid	C21H19BrFN3O3S 492.36	0.99 (LC-3)	493.92	491.98
5-F-I-26a	rac {5-Fluoro-2-[1-(furan-2-carbonyl)-pyrrolidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C19H18FN3O4S 403.43	0.90 (LC-3)	404.08	402.14
5-F-I-27a	rac [2-(1-Butyryl-pyrrolidin-3-ylmethylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid	C18H22FN3O3S 379.45	0.89 (LC-3)	380.12	378.11
5-F-I-28a	rac {5-Fluoro-2-[1-(3-phenyl-propionyl)-pyrrolidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C23H24FN3O3S 441.52	0.99 (LC-3)	442.11	440.17
5-F-I-30a	rac [5-Fluoro-2-(1-octanoyl-pyrrolidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C22H30FN3O3S 435.56	1.08 (LC-3)	436.15	434.21
5-F-I-31a	rac {5-Fluoro-2-[1-(2-phenyl-ethenesulfonyl)-pyrrolidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C22H22FN3O4S2 475.56	1.04 (LC-3)	476.04	474.1
5-F-I-32a	rac {2-[1-(Butane-1-sulfonyl)-pyrrolidin-3-ylmethylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid	C18H24FN3O4S2 429.53	0.99 (LC-3)	430.05	428.18
5-F-I-33a	rac {5-Fluoro-2-[1-(4-methoxy-benzenesulfonyl)-pyrrolidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	C21H22FN3O5S2 479.54	1.01 (LC-3)	480.06	478.12

Table 65

Precursor 5-F-I-36a of the following Table 66 is prepared using a procedure analogous to that described for Precursor I-00a, substituting the corresponding Precursor 5-F-I-25b for Precursor I-00b.

Example	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
5-F-I-36a	[5-Fluoro-2-(pyrrolidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	C14H16FN3O2S 309.36	0.62 (LC-3)	310.12

Table 66

Precursor 5-F-I-25b of the following Table 67 is prepared using a procedure analogous to that described for Precursor I-00b, substituting the corresponding Intermediate 3-III for Intermediate 3-I and 3-hydroxymethyl-pyrrolidin-1-carboxylic acid *tert*-butyl ester for 3-hydroxymethyl-piperidine-1-carboxylic acid *tert*-butyl ester.

Precursor	Name	Formula Mol weight	t_R [min] (Meth.)	MS Data m/z $[M+H]^+$
5-F-I-25b	rac *tert*-Butyl [2-(1-*tert*-butyloxycabonyl-pyrrolidin-3-ylmethylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetate	C23H32FN3O4S 465.58	1.18 (LC-3)	466.28

Table 67

Example Oxy-F-H-11a

rac [2-(5-Acetyl-2-methoxy-phenylmethanesulfinyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid

To a suspension of [2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid (Example 5-F-H-11a, 194 mg, 0.5 mmol) in dichloromethane (3 ml) cooled to 0°C is added *m*-chloroperbenzoic acid (103 mg, 0.6 mmol, 1.2 eq.) and the mixture is stirred at rt for 3 h. The solid is filtered over a fritted funnel and rinsed thoroughly with dichloromethane. The white solid obtained is dried under high vacuum

yielding the title compound (120 mg) in 59% as a white solid: t_R = 0.89 min (LC-3), ESI-MS (pos.): m/z 404.91 $[M+H]^+$; ^{1}H-NMR (DMSO-d_6): δ (ppm) 2.39 (s, 3H, C=OCH_3), 3.65 (s, 3H, OCH_3), 4.66 (dd, 2H, S=OCH_2), 5.20 (d, 2 H, C<u>H</u>CO_2H), 7.11 (d, 1H, $H_{arom.}$), 7.29 (dt, 1 H, $H_{arom.}$), 7.59 (dd, 1 H, $H_{arom.}$), 7.75 (m, 1 H, $H_{arom.}$), 7.98 (dd, 1 H, $H_{arom.}$).

<u>Biological assays</u>:

<u>Preparation of CRTH2 membranes and radioligand binding assay</u>:

Preparation of the membranes and radioligand binding assays are performed according to known procedures, *e.g.* Sawyer N. et al. (*Br. J. Pharmacol.*, 2002, **137**, 1163-1172). A clonal HEK 293 cell line, expressing high level of recombinant hCRTH2 receptor, is selected for the preparation of membranes. Cells are detached from culture plates in 5 ml buffer A per plate (5 mM Tris, 1 mM $MgCl_2$x6 H_2O, 0.1 mM PMSF, 0.1 mM phenanthroline) using a police rubber and transferred into centrifugation tubes and frozen at –80°C. After thawing, the cells are centrifuged at 500 g for 5 min and then resuspended in buffer A. Cells are then fragmented by homogenization with a Polytron homogenizer for 30 s. The membrane fragments are centrifuged at 3000 g for 40 min and resuspended in membranes in buffer B (50 mM Tris, 25 mM $MgCl_2$, 250 mM saccharose, pH 7.4) and aliquots are stored frozen.

Binding assay is performed in a total volume of 250 µl. In each well, 75 µl buffer C [50 mM Tris, 100 mM NaCl, 1 mM EDTA, 0.1% BSA (protease free), 0.01 % NaN_3, pH 7.4] is mixed with 50 µl {^{3}H}-PGD_2 [at 2.5 nM (220.000 dpm per well) from Amersham, TRK734], 100 µl CRTH2 membranes to give 80 µg per well and 25 µl of test compound in buffer C containing 1% DMSO. For unspecific binding, PGD2 is added to the reaction mixture at 1 µM final concentration. This binding assay mix is incubated at rt for 90 min and then filtered through a GF/C filter plate. The filter is washed three times with ice cold binding buffer. Then, 40 µl per well Microscint-40 (Packard) are added and the bound radioactivity is quantified by means of Topcount (Packard).

<u>Test for antagonist binding to the CRTH2 receptor</u>:

Compounds of Formula I display IC_{50} values of less than 10 μM, as exemplified in the following Table 68.

Compound Name	hCRTH2 BDG IC_{50} (μM)
{2-[3-(Butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-5-nitro-benzoimidazol-1-yl}-acetic acid	0.001
{2-[5-Acetyl-2-(3-hydroxy-propoxy)-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid	0.002
[2-(1-Butyryl-piperidin-3-ylmethylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetic acid	0.004
[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-5-formyl-benzoimidazol-1-yl]-acetic acid	0.006
rac. [2-(3-{(2-Cyclohexyl-2-phenyl-acetyl)-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	0.007
[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid	0.009
{2-[3-(Butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid and its sodium salt	0.010
{2-[3-(Pentanoyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid	0.012
rac 2-[2-(5-Acetyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-propionic acid	0.013
(2-{3-[(2,2-Diphenyl-ethyl)-pentanoyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid	0.015
[2-(3-Methoxycarbonyl-benzylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid	0.015
rac. {2-[1-(4-Bromo-benzoyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	0.018
rac. [2-(1-Butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid	0.022
rac {2-[1-(4-Bromo-benzoyl)-pyrrolidin-3-ylmethylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid	0.023

Table 68

Intracellular calcium mobilization assay (FLIPR):

Cells (HEK-293), stably expressing the $hCRTH_2$ receptor under the control of the cytomegalovirus promotor from a single insertion of the expression vector pcDNA5 (Invitrogen), are grown to confluency in DMEM (low glucose, Gibco) medium supplemented with 10% fetal calf serum (both Bioconcept, Switzerland) under standard mammalian cell culture conditions (37°C in a humidified atmosphere of 5% CO_2). Cells are detached from culture dishes using a dissociation buffer (0.02% EDTA in PBS, Gibco) for 1 min, and collected by centrifugation at 200 g at rt for 5 min in assay buffer [equal parts of Hank's BSS (HBSS, Bioconcept) and DMEM (low glucose, without phenol red, Gibco)]. After incubation for 45 min (37°C and 5% CO_2) in the presence of 1 µM Fluo-4 and 0.04% Pluronic F-127 (both Molecular Probes), 20 mM HEPES (Gibco) in assay buffer, the cells are washed with and resuspended in assay buffer, then seeded onto 384-well FLIPR assay plates (Greiner) at 50,000 cells in 66 µl per well, and sedimented by centrifugation.

Stock solutions of test compounds are made up at a concentration of 10 mM in DMSO, and serially diluted in assay buffer to concentrations required for inhibition dose response curves. Prostaglandin D_2 (Biomol, Plymouth Meeting, PA) is used as an agonist.

A FLIPR384 instrument (Molecular Devices) is operated according to the manufacturer's standard instructions, adding 4 µl of test compound dissolved at 10 mM in DMSO and diluted prior to the experiment in assay buffer to obtain the desired final concentration. An assay buffer containing 10 µl of 80 nM prostaglandin D_2 (Biomol, Plymouth Meeting, PA), supplemented with 0.8% bovine serum albumin (fatty acid content <0.02%, Sigma), is then added to obtain a final concentration of 10 nM and 0.1%, respectively. Changes in fluorescence are monitored before and after the addition of test compounds at λ_{ex}=488 nm and λ_{em}=540 nm. Emission peak values above base level after prostaglandin D_2 addition are exported after base line subtraction. Values are normalized to high-level control (no test compound added) after subtraction of base line value (no prostaglandin D_2 added). The program XLlfit 3.0 (IDBS) is used to fit

the data to a single site dose response curve of the equation (A+((B-A)/(1+((C/x)^D)))) and to calculate the IC_{50} values.

Antagonist analysis:

Compounds of Formula I antagonize prostaglandin D2 mediated hCRTH2 receptor activity with an IC_{50} of less than 10 μM as exemplified in the following Table 69.

Compound Name	hCRTH2 FLIPR IC_{50} (μM)
{2-[5-(2,3-Dihydro-indole-1-carbonyl)-2-methoxy-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid	0.004
[2-(3-Methoxycarbonyl-benzylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid	0.015
[2-(5-Butylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid	0.021
rac {2-[1-(4-Bromo-benzoyl)-pyrrolidin-3-ylmethylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid	0.088
[2-(3-Methoxycarbonyl-benzylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetic acid and its 6 trifluoromethyl regioisomer	0.098
[2-(3-{Diphenylpropionyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid	0.128
[2-(1-Butyryl-piperidin-3-ylmethylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetic acid	0.148

rac {2-[1-(3-Chloro-benzoyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid	0.156
{2-[(6-Methoxy-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid	0.201
[2-(3,3-Diphenyl-propylsulfanyl)-6-nitro-benzoimidazol-1-yl]-acetic acid	0.212

Table 69

Formulations:

The compounds of the invention can be formulated as the active ingredient according to methods known per se to give e.g. pharmaceutical preparations of the following composition:

1. 500 mg tablets

Active ingredient	500 mg
Powdered lactose	149 mg
Polyvinylpyrrolidone	15 mg
Dioctyl sodium sulfosuccinate	1 mg
Sodium carboxymethyl starch	30 mg
Magnesium stearate	5 mg
Total	700 mg

2. 50 mg tablets

Active ingredient	50 mg
Powdered lactose	50 mg
Microcrystalline cellulose	82 mg
Sodium carboxymethyl starch	15 mg
Total	200 mg

3. 100 mg capsules

Active ingredient	100.0 mg
Powdered lactose	104.7 mg
Corn starch	70.0 mg
Hydroxypropylmethyl cellulose	10.0 mg
Dioctyl sodium sulfosuccinate	0.3 mg
Talc	12.0 mg
Magnesium stearate	3.0 mg
	Total 300.0 mg

4. 500 mg suppositories

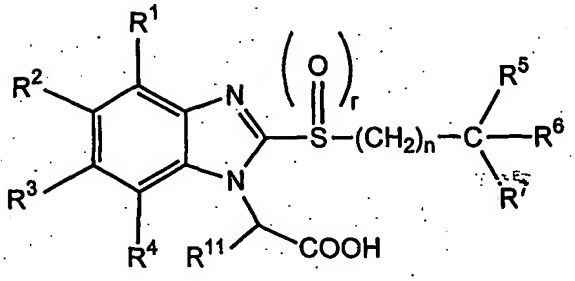
Active ingredient	500 mg
Suppository mass	ad 2000 mg

5. 100 mg soft gelatine capsules

Active ingredient	100 mg
Medium chain triglyceride	300 mg
	Total 400 mg

CLAIMS

1. Use of a compound selected from the group consisting of 2-sulfanyl-benzoimidazol-1-yl-acetic acids of the general Formula I



I

wherein

R^1, R^2, R^3 and R^4 each independently represent hydrogen; alkyl; haloalkyl; halogen; nitro; cyano; formyl; methylsulfonyl; or methylcarbonyl;

n is 0 or an integer from 1 to 10;

r is 0 or the integer 1;

R^5, R^6 and R^7 each independently represent hydrogen; alkyl; alkenyl; cycloalkyl; aryl; aryloxy; alkylcarbonyl; cycloalkylcarbonyl; alkoxycarbonyl, arylcarbonyl; arylalkylcarbonyl; N-alkyl-N-aryl-carbamoyl; N-alkyl-N-arylalkyl-carbamoyl; N-arylalkyl-N-aryl-carbamoyl; heterocyclyl; heterocyclyloxy; heterocyclylcarbonyl; or an amino of Formula NR^8R^9; or two of R^5-R^7 together with the carbon atom to which they are attached form cycloalkyl or saturated heterocyclyl;

R^8 represents hydrogen or R^9;

R^9 independently from R^8 represents cycloalkyl; cycloalkylalkyl; aryl; cycloalkylarylalkyl; arylalkyl; (diaryl)-alkyl; alkylcarbonyl; alkenylcarbonyl; cycloalkylcarbonyl; cycloalkylalkylcarbonyl; alkoxycarbonyl; alkoxydicarbonyl; arylcarbonyl; arylalkylcarbonyl; arylalkenylcarbonyl; (diaryl)-alkylcarbonyl; cycloalkylarylalkylcarbonyl; heterocyclylcarbonyl; alkylcarbamoyl; arylcarbamoyl; arylalkylcarbamoyl; alkylsulfonyl; arylsulfonyl; arylalkylsulfonyl; or

R^8 and R^9, together with the nitrogen atom to which they are attached, form a heterocyclyl group;

R^{11} is hydrogen or methyl;

and optically pure enantiomers, mixtures of enantiomers, racemates, optically pure diastereoisomers, mixtures of diastereoisomers, diastereoisomeric racemates, mixtures of diastereoisomeric racemates, meso forms, geometric isomers, and prodrugs of compounds in which a prodrug forming group is present, as well as solvates and pharmaceutically acceptable salts of such compounds, and morphological forms;

for the manufacture of medicaments for the control of disorders responding to CRTH2 receptor antagonist treatment.

2. The use of a compound of Formula I according to claim 1, wherein R^1, R^2, R^3 and R^4 each independently represent hydrogen, alkyl, haloalkyl, halogen, nitro, cyano or formyl; r is 0; and R^{11} is hydrogen.

3. Compounds as defined in Claim 1 or 2 for use as therapeutically active substances, with the exception of {2-[3-methyl-4-(2-morpholin-4-yl-ethylsulfanyl)-pyridin-2-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid.

4. A medicament containing one or more compounds according to Claim 3 and a pharmaceutically acceptable carrier.

5. Compounds as defined in Claim 1 or 2, with the exception of:

(2-octylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-butylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-propylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-ethylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-methylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-isopropylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-*sec*-butylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-isobutylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-allylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-cyclohexylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-benzylsulfanyl-benzoimidazol-1-yl)-acetic acid;

(2-phenethylsulfanyl-benzoimidazol-1-yl)-acetic acid;

[2-(naphthalen-1-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[2-(4-*tert*-butyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-propoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-ethoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(3,4-dimethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(3-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(naphthalen-2-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-methoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-butoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[2-(4-ethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-isopropyl-4-methyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(naphthalen-1-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2,6-Dimethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(4-isopropoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-fluoro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[2-(2-methoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

and

{2-[3-methyl-4-(2-morpholin-4-yl-ethylsulfanyl)-pyridin-2-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid.

6. Compounds according to Claim 5, wherein

R^5 represents hydrogen;

R^6 represents hydrogen; alkyl; or alkoxycarbonyl; and

R^7 represents alkoxycarbonyl; N-alkyl-N-arylalkyl-carbamoyl; N-alkyl-N-aryl-carbamoyl; alkylcarbonyl; N-arylalkyl-N-aryl-carbamoyl; arylalkylcarbonyl; arylcarbonyl; cycloalkylcarbonyl; heterocyclylcarbonyl; heterocyclyloxy; an amino of Formula NR^8R^9; aryl substituted with one or two of alkoxy, alkylcarbonyl, and alkoxycarbonyl and optionally an additional halogen; or heterocyclyl substituted with alkylcarbonyl, cycloalkylcarbonyl, alkoxycarbonyl, arylcarbonyl, arylalkylcarbonyl, (diaryl)alkyl carbonyl or heterocyclylcarbonyl and optionally an additional halogen; or

R^6 represents alkyl or alkoxycarbonyl and R^7 represents aryl; or

R^6 and R^7 together with the carbon atom to which they are attached form cycloalkyl or saturated heterocyclyl.

7. Compounds according to Claim 1, wherein

R^1, R^2, R^3 and R^4 each independently represent hydrogen; alkyl; haloalkyl; halogen; nitro; cyano; formyl; methylsulfonyl; or methylcarbonyl;

n is 0 or an integer from 1 to 5;

r is 0 or the integer 1;

R^5, R^6 and R^7 each independently represent hydrogen; alkyl; alkenyl; cycloalkyl; aryl; aryloxy; alkoxycarbonyl, arylcarbonyl; N-alkyl-N-aryl-carbamoyl; N-alkyl-N-arylalkyl-carbamoyl; N-arylalkyl-N-aryl-carbamoyl; heterocyclyl; heterocyclyloxy; heterocyclylcarbonyl; or an amino of Formula NR^8R^9; or two of R^5-R^7 together with the carbon atom to which they are attached form cycloalkyl or saturated heterocyclyl;

R^8 represents hydrogen or R^9;

R^9 independently from R^8 represents cycloalkyl; cycloalkylalkyl; aryl; arylalkyl; (diaryl)-alkyl; alkylcarbonyl; cycloalkylcarbonyl; cycloalkylalkylcarbonyl; alkoxycarbonyl; alkoxydicarbonyl; arylcarbonyl; arylalkylcarbonyl; arylalkenylcarbonyl; (diaryl)-alkylcarbonyl; heterocyclylcarbonyl; alkylcarbamoyl; arylcarbamoyl; arylalkylcarbamoyl; alkylsulfonyl; arylsulfonyl; arylalkylsulfonyl; or R^8 and R^9, together with the nitrogen atom to which they are attached, form a heterocyclyl group; and

R^{11} is hydrogen or methyl;

with the exception of the following compounds:

(2-octylsulfanyl-benzoimidazol-1-yl)-acetic acid;
(2-butylsulfanyl-benzoimidazol-1-yl)-acetic acid;
(2-propylsulfanyl-benzoimidazol-1-yl)-acetic acid;
(2-ethylsulfanyl-benzoimidazol-1-yl)-acetic acid;
(2-methylsulfanyl-benzoimidazol-1-yl)-acetic acid;
(2-isopropylsulfanyl-benzoimidazol-1-yl)-acetic acid;
(2-*sec*-butylsulfanyl-benzoimidazol-1-yl)-acetic acid;
(2-isobutylsulfanyl-benzoimidazol-1-yl)-acetic acid;
(2-allylsulfanyl-benzoimidazol-1-yl)-acetic acid;
(2-cyclohexylsulfanyl-benzoimidazol-1-yl)-acetic acid;
(2-benzylsulfanyl-benzoimidazol-1-yl)-acetic acid;
(2-phenethylsulfanyl-benzoimidazol-1-yl)-acetic acid;
[2-(naphthalen-1-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[2-(4-*tert*-butyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(4-propoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(4-ethoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(3,4-dimethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(3-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(naphthalen-2-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(4-methoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(4-butoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(4-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
[2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[2-(4-ethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(2-methylphenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(2-isopropyl-4-methyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(naphthalen-1-yloxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(2,6-Dimethyl-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(4-isopropoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(2-fluoro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[2-(2-methoxy-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
and
{2-[3-methyl-4-(2-morpholin-4-yl-ethylsulfanyl)-pyridin-2-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid.

8. Compounds according to Claim 5 or 7, wherein aryl groups present as R^5-R^9, alone or in combination, are unsubstituted or mono- or di-substituted with substituents independently selected from lower alkyl; hydroxy-lower alkyl; lower alkoxy; lower alkoxy-lower alkyl; halogen; cyano; lower alkoxycarbonyl; lower alkylcarbonyl; aryl; aryl-lower alkyl; cycloalkyl; 2,3-dihydro-indole-1-carbonyl; lower alkylcarbamoyl; morpholine-4-carbonyl; aryl-lower alkylcarbamoyl; N,N-di-lower alkylcarbamoyl; N-lower alkyl-N-aryl-lower alkyl-carbamoyl; hydroxy-lower alkoxy; arylcarbonyl; and heterocyclyl.

9. Compounds according to any one of Claims 5-8, wherein R^6 and R^7 together with the carbon atom, to which they are attached, form a saturated heterocyclyl ring containing one nitrogen atom which is substituted with R^{10}, wherein R^{10} represents alkylcarbamoyl; alkylcarbonyl; alkoxycarbonyl; alkylsulfonyl; arylalkylcarbamoyl; arylalkylcarbonyl; arylalkoxycarbonyl; arylalkylsulfonyl; arylcarbamoyl; arylcarbonyl; (diaryl)-alkylcarbonyl; aryloxycarbonyl; arylsulfonyl; arylalkenylsulfonyl; cycloalkylcarbamoyl; cycloalkylalkylcarbonyl; cycloalkylcarbonyl; cycloalkyloxycarbonyl; cycloalkylsulfonyl; heterocyclylcarbamoyl; heterocyclylcarbonyl; heterocyclyloxycarbonyl; or heterocyclylsulfonyl.

10. Compounds according to any one of Claims 5-9, wherein R^1, R^2, R^3 and R^4 each independently represent hydrogen; methyl; trifluoromethyl; fluoro, chloro, bromo; nitro; cyano; or formyl.

11. Compounds according to any one of Claims 5-10, wherein n is 1 or 2; R^5 and R^6 each represent hydrogen; R^7 represents an amino of Formula NR^8R^9;

R^8 represents hydrogen; and
R^9 represents cycloalkyl; aryl; arylalkyl; (diaryl)-alkyl; alkylcarbonyl; cycloalkyl-alkylcarbonyl; cycloalkylcarbonyl; alkenylcarbonyl; alkoxycarbonyl; alkoxydicarbonyl; arylcarbonyl; arylalkylcarbonyl; (diaryl)-alkylcarbonyl; heterocyclylcarbonyl; alkylcarbamoyl; arylcarbamoyl; arylalkylcarbamoyl; alkylsulfonyl; arylsulfonyl; arylalkylsulfonyl; or

R^8 represents cycloalkyl; arylalkyl; aryl; alkoxycarbonyl; and
R^9 represents cycloalkyl; cyclylalkyl-alkyl; aryl; arylalkyl; (diaryl)-alkyl; cycloalkyl-alkylcarbonyl; alkylcarbonyl; arylalkylcarbonyl; (diaryl)-alkylcarbonyl; alkylcarbamoyl; arylcarbamoyl; arylalkylcarbamoyl; alkylsulfonyl; arylsulfonyl; arylalkylsulfonyl; or

R^8 and R^9, together with the nitrogen atom to which they are attached, form a phthalazinyl; isoindolyl; benzoimidazolyl; indazolyl; quinazolinyl; or benzoisothiazolyl ring system.

12. Compounds according to Claim 11, wherein R^8 represents hydrogen; and R^9 represents 3-phenyl-acryloyl; butoxycarbonyl, *tert*-butoxycarbonyl; ethoxydicarbonyl; propylcarbamoyl; 2,2-dimethyl-propionyl; 3,3-dimethyl-butyryl, 3-octanoyl, pentanoyl; butane-1-sulfonyl; 4-piperidin-1-yl-phenyl, phenyl; 2,2-diphenyl-ethyl, 3-benzyl; 2-cyclohexyl-2-phenyl-acetyl, 3,3-diphenyl-propionyl, 3-phenyl-propionyl, diphenylacetyl, phenylacetyl; phenylmethanesulfonyl; phenylcarbamoyl; 4-bromo-benzoyl, 4-methoxy-benzoyl, benzoyl, biphenyl-4-carbonyl, naphthalene-1-

carbonyl, benzenesulfonyl; cyclohexanecarbonyl, cyclopropanecarbonyl, 3-cyclopentyl-propionyl; furan-2-carbonyl, or pyridine-3-carbonyl; or

R^8 represents butoxycarbonyl, *tert*-butoxycarbonyl; 4-carboethoxyphenyl, 4-piperidin-1-yl-phenyl, phenyl; benzyl, 2,2-diphenyl-ethyl, phenethyl; cyclopropyl; and

R^9 represents propylcarbamoyl; pentanoyl; butane-1-sulfonyl; 4-piperidin-1-yl-phenyl, phenyl; benzyl, phenethyl, 2,2-diphenyl-ethyl; benzylcarbamoyl; 2-cyclohexyl-2-phenyl-acetyl, 2-phenylacetyl, 3,3-diphenyl-propionyl, diphenylacetyl, phenylmethanesulfonyl; phenylcarbamoyl; benzenesulfonyl; cyclohexyl, cyclopropyl; or cyclohexylmethyl; or

R^8 and R^9, together with the nitrogen atom to which they are attached, represent 1-oxo-1*H*-phthalazin-2-yl; 1-oxo-1,3-dihydro-isoindol-2-yl; 2-oxo-2,3-dihydro-benzoimidazol-1-yl; 1-ethoxycarbonyl-3-oxo-2,3-dihydro-indazole-2-yl; 2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-yl; or 1,3-dioxo-1,3-dihydro-isoindol-2-yl; 1,1,3-trioxo-1,3-dihydro-1λ^6-benzo[d]isothiazol-2-yl.

13. Compounds according to any one of Claims 5-10, wherein n is 0; R^5 and R^6 each represent hydrogen; and R^7 represents phenyl; furanyl, oxazolyl, pyridinyl or thiazolyl, all substituted with one or two of alkoxy, alkylcarbonyl, and alkoxycarbonyl and optionally an additional halogen.

14. Compounds according to any one of Claims 5-10, wherein n is 0; R^5 and R^6 each represent hydrogen; and R^7 represents phenyl, optionally mono- or di-substituted wherein the substitutents are independently selected from the group consisting of hydroxy-alkyl, alkoxy, alkoxyalkyl, alkoxycarbonyl, halo, alkylcarbonyl, phenyl, 2,3-dihydro-indole-1-carbonyl, alkylcarbamoyl, morpholine-4-carbonyl, benzylcarbamoyl, N,N-dialkylcarbamoyl, N-alkyl-N-benzyl-carbamoyl, hydroxyalkoxy and benzoyl; or R^7 represents 3-oxo-indan-5-yl or 8-oxo-5,6,7,8-tetrahydro-naphthalen-2-yl, both substituted by alkoxy.

15. Compounds according to any one of Claims 5-10, wherein n is 1; R^5 represents hydrogen; and R^6 and R^7 together with the carbon atom to which they are attached form a 5- or 6-membered saturated heterocyclyl containing one nitrogen ring

atom, wherein this nitrogen ring atom contains a substituent R^{10}, wherein R^{10} is as defined in Claim 9.

16. Compounds according to Claim 5 selected from the group consisting of:

{2-[3-(butoxycarbonyl-phenethyl-amino)-propylsulfanyl]-5-nitro-benzoimidazol-1-yl}-acetic acid;

rac [2-(3-{(2-cyclohexyl-2-phenyl-acetyl)-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

(2-{3-[(2,2-diphenyl-ethyl)-pentanoyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

[2-(3-methoxycarbonyl-benzylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid;

rac {2-[1-(4-bromo-benzoyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[(6-methoxy-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[5-fluoro-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-fluoro regioisomer;

{2-[(6-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(3-{butyloxycarbonyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[5-cyano-2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-cyano regioisomer;

[2-(4-ethyloxycarbonyl-butylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid;

[2-(3-{diphenylacetyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(3-{[(4-ethyloxycarbonyl)-phenyl]-pentanoyl-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

rac {2-[1-(furan-2-carbonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(benzyl-butoxycarbonyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(3-phenyl-propionyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[(4-ethyloxycarbonylphenyl)-(phenylacetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(benzyl-pentanoyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(cyclopropyl-diphenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(3-{diphenylpropionyl-[(4-ethyloxycarbonyl)-phenyl]-amino}-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

rac [2-(1-methyl-2-oxo-2-phenyl-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(3-methoxycarbonyl-benzylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetic acid and its 6-trifluoromethyl regioisomer;

[2-(3,3-diphenyl-propylsulfanyl)-6-nitro-benzoimidazol-1-yl]-acetic acid;

(2-benzylsulfanyl-5-nitro-benzoimidazol-1-yl)-acetic acid and its 6-nitro isomer;

{2-[3-(1-phenethyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(3-chloro-benzoyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-5-nitro-benzoimidazol-1-yl}-acetic acid;

{2-[3-(1,1,3-trioxo-1,3-dihydro-1λ^6-benzo[d]isothiazol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[(2,2-diphenyl-ethyl)-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

(2-{3-[cyclopropyl-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

rac (2-{3-[(2-cyclohexyl-2-phenyl-acetyl)-cyclopropyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

(2-{3-[diphenylacetyl-(2,2-diphenyl-ethyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

rac [2-(1-heptanoyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[3-(3,3-diphenyl-propionylamino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[(butane-1-sulfonyl)-phenethyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(benzyl-(phenylmethanesulfonyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[(2,2-diphenyl-ethyl)-(phenylacetyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(benzenesulfonyl-cyclopropyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(phenethyl-(phenylmethanesulfonyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(3,3-diphenyl-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

{2-[3-(phenethyl-(phenylacetyl)amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(diphenylacetyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{[(2-chloro-4-methyloxycarbonyl)-pyridin-6-yl]-methyl-sulfanyl}-benzoimidazol-1-yl)-acetic acid;

rac [2-(bicyclo[4.2.0]octa-1,3,5-trien-7-ylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(3-acetyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[5-fluoro-2-(2-phenoxy-ethylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-fluoro regioisomer;

[2-(3-phenylmethanesulfonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(4-ethyloxycarbonyl-butylsulfanyl)-6-nitro-benzoimidazol-1-yl]-acetic acid;

{2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[3-(1,3-dioxo-1,3-dihydro-isoindol-2-yl)-propylsulfanyl]-6-nitro-benzoimidazol-1-yl}-acetic acid;

(2-{3-[phenylmethanesulfonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

[2-(4-ethyloxycarbonyl-butylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid and its 6-fluoro regioisomer;

[2-(3-diphenylacetylamino-propylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid;

{2-[3-(cyclopropyl-(phenylmethanesulfonyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

{2-[(5-bromo-3-methoxycarbonyl)-benzylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{5-nitro-2-[2-(4-chloro-phenoxy)-ethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
[2-(3,3-diphenyl-propylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid;
{2-[3-(2,4-dioxo-1,4-dihydro-2*H*-quinazolin-3-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[3-(benzyl-(phenylacetyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
(2-{3-[(2,2-diphenyl-ethyl)-(phenylmethanesulfonyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
rac [2-(1-acetyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
(2-{3-[benzyl-(3,3-diphenyl-propionyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
{2-[3-(cyclopropyl-(phenylacetyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
rac [2-(1-methyloxycarbonyl-1-phenyl-methylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[3-(butoxycarbonyl-cyclohexyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
[2-(3-diphenylacetylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[3-(1,3-diphenyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
(2-benzylsulfanyl-6-nitro-benzoimidazol-1-yl)-acetic acid;
rac [2-(1-diphenylacetyl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[3-(cyclopropyl-pentanoyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
(2-{3-[benzenesulfonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;
{2-[3-(benzyl-diphenylacetyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
{2-[3-(*tert*-butoxycarbonyl-phenyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;
[2-(3-phenyl-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
[2-(3-methoxycarbonyl-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
[2-(3-benzenesulfonylamino-propylsulfanyl)-benzoimidazol-1-yl]-acetic acid;
{2-[3-(1-benzyl-3-propyl-ureido)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[1-(2,2-diphenyl-ethyl)-3-propyl-ureido]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

[2-(4-ethyloxycarbonyl-butylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetic acid and its 6-trifluoromethyl regioisomer;

[5-cyano-2-(4-ethyloxycarbonyl-butylsulfanyl)-benzoimidazol-1-yl]-acetic acid and its 6-cyano regioisomer;

[2-(5-ethyloxycarbonyl-pentylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

(2-{3-[(3,3-diphenyl-propionyl)-phenyl-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(butoxycarbonyl-(cyclohexylmethyl)-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[*tert*-butoxycarbonyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

(2-{3-[phenylacetyl-(4-piperidin-1-yl-phenyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(2,3-dihydro-1-ethyloxycarbonyl-3-oxo-indazol-2-yl)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(3-cyclopentyl-propionyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

(2-{3-[*tert*-butoxycarbonyl-(2,2-diphenyl-ethyl)-amino]-propylsulfanyl}-benzoimidazol-1-yl)-acetic acid;

{2-[3-(benzenesulfonyl-phenethyl-amino)-propylsulfanyl]-benzoimidazol-1-yl}-acetic acid; and

{2-[5-(3,4-dihydro-2*H*-quinolin-1-yl)-5-oxo-pentylsulfanyl]-benzoimidazol-1-yl}-acetic acid.

17. Compounds according to Claim 1 selected from the group consisting of:

rac {2-[1-(3,4-dichloro-benzenesulfonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(3-phenyl-acryloyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-5,6-dimethyl-benzoimidazol-1-yl]-acetic acid;

[2-(5-methyloxycarbonyl-benzylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetic acid;

[2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-5,6-dichloro-benzoimidazol-1-yl]-acetic acid;

[2-((R)-1-butyryl-piperidin-3-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5,6-difluoro-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

rac [2-(1-butyryl-piperidin-3-ylmethylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

rac {5-fluoro-2-[1-(furan-2-carbonyl)-piperidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {2-[1-(4-bromo-benzoyl)-piperidin-3-ylmethylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-trifluoromethyl-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-methanesulfonyl-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-6-fluoro-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-4-fluoro-benzoimidazol-1-yl]-acetic acid;

[5-acetyl-2-(5-acetyl-2-methoxy-benzylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-formyl-benzoimidazol-1-yl]-acetic acid;

rac 2-[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-propionic acid;

[2-(5-butylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

[2-(5-benzylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

{2-[5-(2,3-dihydro-indole-1-carbonyl)-2-methoxy-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid;

[2-(5-diethylcarbamoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-methoxy-benzylsulfanyl)-5-nitro-benzoimidazol-1-yl]-acetic acid;

rac {2-[1-(4-bromo-benzoyl)-pyrrolidin-3-ylmethylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid;

rac {5-fluoro-2-[1-(furan-2-carbonyl)-pyrrolidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

rac {5-fluoro-2-[1-(2-phenyl-ethenesulfonyl)-pyrrolidin-3-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetic acid;

[2-(5-acetyl-2-butoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

{2-[5-acetyl-2-(3-hydroxy-propoxy)-benzylsulfanyl]-5-fluoro-benzoimidazol-1-yl}-acetic acid;

[2-(5-benzoyl-2-methoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

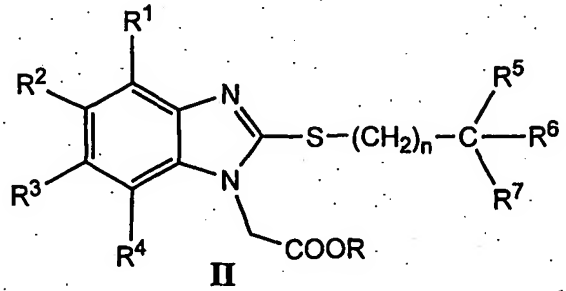
[5-fluoro-2-(6-methoxy-3-oxo-indan-5-ylmethylsulfanyl)-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-ethoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid;

[2-(5-acetyl-2-propoxy-benzylsulfanyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid; and

rac [2-(5-acetyl-2-methoxy-phenylmethanesulfinyl)-5-fluoro-benzoimidazol-1-yl]-acetic acid.

18. Compounds of the general Formula II



II

wherein R^1-R^7 and n are as in Formula I and R represents an alkyl group, with the exception of:

methyl [2-(5-trifluoromethyl-pyridin-2-ylsulfanyl)-benzoimidazol-1-yl]-acetate;

methyl [2-(4-chloro-benzylsulfanyl)-benzoimidazol-1-yl]-acetate;

methyl (2-benzylsulfanyl-benzoimidazol-1-yl)-acetate;

methyl [2-(5-nitro-pyridin-2-ylsulfanyl)-benzoimidazol-1-yl]-acetate;

methyl (2-methylsulfanyl-benzoimidazol-1-yl)-acetate;

ethyl (2-methylsulfanyl-benzoimidazol-1-yl)-acetate;

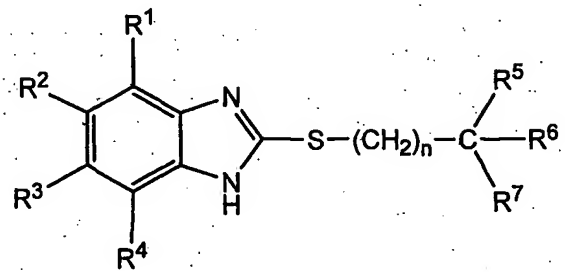
methyl (2-ethylsulfanyl-benzoimidazol-1-yl)-acetate;

ethyl [2-(1,3,7-trimethyl-2,6-dioxo-2,3,6,7-tetrahydro-1*H*-purin-8-ylsulfanyl)-benzoimidazol-1-yl]-acetate;

ethyl {2-[3-methyl-4-(2-morpholin-4-yl-ethylsulfanyl)-pyridin-2-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate; and

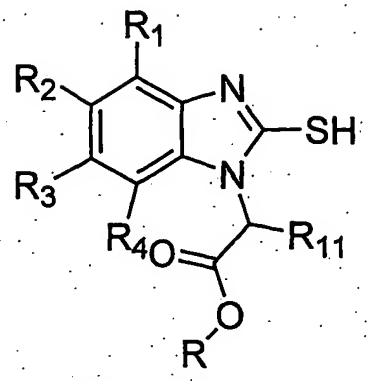
methyl {2-[3-methyl-4-(2-morpholin-4-yl-ethylsulfanyl)-pyridin-2-ylmethylsulfanyl]-benzoimidazol-1-yl}-acetate.

19. Compounds of the general Formula



wherein R^1-R^7 and n are as in Formula I.

20. Compounds of the general Formula



wherein R^1-R^4 and R^{11} are as defined for Formula I and R represents an alkyl group.

21. Compounds as defined in Claim 5 for use as therapeutically active substances.

22. A medicament containing one or more compounds according to Claim 5 and a pharmaceutically acceptable carrier.

23. The use of compounds according to Claim 5 for the manufacture of medicaments for the control of disorders responding to CRTH2 receptor antagonist treatment.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/009083

A. CLASSIFICATION OF SUBJECT MATTER
A61K31/4184 A61K31/425 A61K31/4439 A61K31/445 A61K31/4709
A61P1/00 A61P1/04 A61P5/00 A61P9/00 A61P9/10
A61P11/00 A61P11/06 A61P17/00 A61P19/02 A61P27/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data, MEDLINE, EMBASE, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	DATABASE HCAPLUS 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; LABANAUSKAS, L K ET AL.: "Synthesis and antiphlogistic activity of novel 5,6-dialkoxy-2-mercaptobenzimidazolylaceti c acid derivatives" XP002357548 retrieved from STN Database accession no. 1998:342082 abstract & KHIMIKO-FARMATSEVTICHESKII ZHURNAL, vol. 32, no. 2, 1998, pages 15-16, -/--	1-23

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
6 December 2005	18/01/2006

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Taylor, G.M.

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	-& DATABASE REGISTRY STN; CAS Registry Number: 209327-35-5 2 August 1998 (1998-08-02), "1H-Benzimidazole-1-acetic acid, 5,6-diethoxy-2-(ethylthio)-" XP002362212 abstract -& DATABASE REGISTRY STN; CAS Registry Number: 209327-33-3 2 August 1998 (1998-08-02), "1H-Benzimidazole-1-acetic acid, 2-(ethylthio)-5,6-dimethoxy-" XP002362213 abstract	
X	EP 0 167 943 A (BEECHAM GROUP PLC) 15 January 1986 (1986-01-15) abstract page 1, line 1 - page 5 page 27, paragraph 4 examples 1-31 claims 1-14	1-17,19
X	HUANG, N; NAGARSEKAR, A; XIA, G; HAYASHI, J; MACKERELL, A D: "Identification of Non-Phosphate-Containing Small Molecular Weight Inhibitors of the Tyrosine Kinase p56 Lck SH2 Domain via in Silico Screening against the pY + 3 Binding Site" J. MED. CHEM., vol. 47, 6 April 2004 (2004-04-06), pages 3502-3511, XP002357544 cited in the application Published on the Web: 06/04/2004 abstract Figure 6, compound #201 page 3510, last paragraph	1-4,7,18
X	GB 1 152 814 A (LABORATOIRES CASSENNE) 21 May 1969 (1969-05-21) the whole document	19
X	DATABASE WPI Week 199213 Derwent Publications Ltd., London, GB; AN 1992-101154 XP002357505 "New silver halide photograph material contains specific diazole compound" & JP 04 044036 A (KONICA CORP) 13 February 1992 (1992-02-13) abstract & DATABASE REGISTRY STN; CAS Registry Number: 141720-30-1 "1H-Benzimidazole-1-acetic acid, 2,3-dihydro-2-thioxo-, methyl ester"	20

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2005/009083

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 2005/094816 A (ACTELION PHARMACEUTICALS LTD; FECHER, ANJA; FRETZ, HEINZ; HILPERT, KUR) 13 October 2005 (2005-10-13) abstract claims 1-16	1-23
P,X	WO 2005/060956 A (UNIVERSITY OF MARYLAND, BALTIMORE; MACKERELL, ALEXANDER, D., JR; HAYAS) 7 July 2005 (2005-07-07) abstract page 200, compound #201 claims 1-23	1-23

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP2005/009083

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		DE 1695353 A1	18-03-1971
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		US 3558775 A	26-01-1971
JP 4044036 A	13-02-1992	NONE	
WO 2005094816 A	13-10-2005	NONE	
WO 2005060956 A	07-07-2005	AU 2003297904 A1	14-07-2005